Synthesis of L-Furanomycin and Its Analogues via Furoisoxazolines[‡][‡‡]

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Dedicated to Professor Franz Effenberger on the occasion of his 75th birthday

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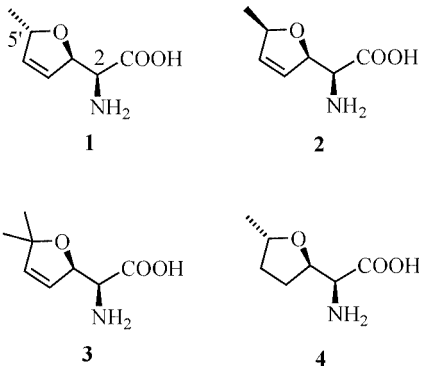
The 1,3-dipolar cycloaddition of nitrile oxides and 2-methylfuran has provided suitable precursors for α-amino acids such as L-furanomycin (**1**) that contain a dihydrofuran ring. By using a chiral nitrile oxide derived from D-glyceraldehyde, the enantiomerically pure furoisoxazolines **9** and **10** were obtained. Owing to the bicyclic, bowl-shaped structure of furoisoxazoline **9** highly stereoselective additions were feasible, in particular, the epoxidation of **9** with dimethyldioxirane provided the required (5′*S*) configuration in **1** after epoxide reduction. Hydroboration of **9** led to the (5′*R*) epimer **2** and nucleophilic addition of a methyl Grignard reagent to epoxyfuroisoxazoline **11** gave rise to 5′-methylfuranomycin (**3**). Further, catalytic hydrogenation of the dihydrofuran intermediate **22**, derived from **11**, afforded the tetrahydrofuranyl derivative **31** from which dihydrofuranomycin (**4**) was obtained in enantiomerically pure form. The biological activities of these α-amino acids showed an extremely narrow structure–activity profile, the natural product being the only compound of this series with high activities.

Introduction

L-(+)-Furanomycin (**1**) is a naturally occurring α-amino acid that was isolated from *Streptomyces threomyceticus* (ATCC 15795) in 1967 by Katagiri et al.[3] Furanomycin (**1**) shows antibiotic activity against several bacterial species;[3] later it was found to be a substrate of isoleucyl aminoacyl tRNA synthetase derived from *E. coli*, which incorporates **1** in vitro into proteins instead of isoleucine.[4] NMR studies have indicated that the conformation of enzyme-bound furanomycin is very similar to the isoleucine analogue, although the structures of these two amino acids differ considerably.[5] The translation ability of this unusual α-amino acid into the protein is also of particular interest with regard to protein engineering.[6]

Parry and co-workers have reported on labelling experiments in the biogenesis of L-furanomycin (**1**).[7,8] It was suggested that the diepoxide of heptadienoic acid is transformed into an allylic alcohol after epoxide opening and that the hydroxy group then attacks the second epoxide to form the dihydrofuran ring. Further biotransformations of this dihydrofuran intermediate lead to the amino acid **1**.



Until now, five enantioselective syntheses of L-(+)-furanomycin **1** have been published; the first one in 1980 by Joullié and co-workers starting from D-glucose[9] established the correct absolute configuration of **1**. This was confirmed later by crystal structure analysis of the *N*-acetyl derivative.[10] The groups of Kang and Clive reported on syntheses of **1** starting from dimethyl L-tartrate[11] and from L-xylose,[12] respectively. Van Brunt and Standaert presented a short synthesis of **1** based on the Ag^{I}-catalyzed cyclization of an allenic alcohol.[6] In addition, several strategies for approaches to stereoisomers of **1**, such as 5′-*epi*-furanomycin (**2**), involving the use of substituted furans[9] and carbohydrate precursors,[9,13,14] have been advanced. In order to clarify the structure–activity relationship of compounds in this series, a number of racemic furanomycin analogues,

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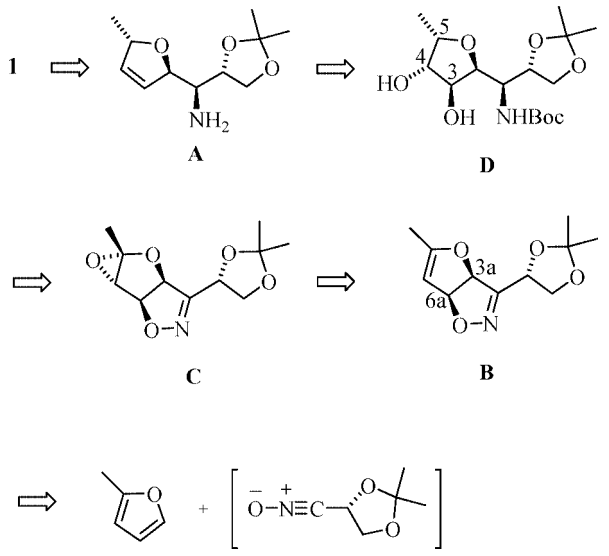
such as norfuranomycin, 3-methyl, 4-methyl, and α-methyl regioisomers of furanomycin, cyclopentylglycine, and cyclopentenylglycine, were synthesized by Kazmaier et al. based on aldol reactions and ring-closing metathesis or ester enolate Claisen rearrangement.[15] In a preliminary communication in 2000 we reported on the synthesis of enantiomerically pure **1**, its 5′-epimer **2**, and the 5′-methyl derivative **3** starting with a 1,3-dipolar cycloaddition reaction of a suitable nitrile oxide and 2-methylfuran.[16] In this paper we now give details of this approach, along with those for the synthesis of L-dihydrofuranomycin (**4**). The preparation of analogues **2**–**4** seemed of particular interest in view of the biological activities of the parent compound **1**.

Results and Discussion

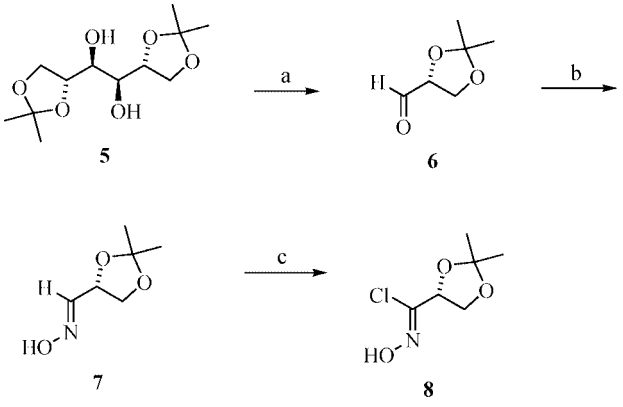
The strategy for the synthesis of **1** is shown in Scheme 1. It was planned that the carboxy group in the target structure would be introduced into an early reaction intermediate as a diol-acetonide with the nitrile oxide, which would be conveyed through all the steps of the synthesis and be set free at the end. The relative configuration at C2/C2′ (*threo*) would result from furoisoxazoline reduction, as experienced earlier.[17–20] The 2,5-*trans*-disubstituted dihydrofuryl part in **A** might be formed from **B** by S_N2' hydride addition which would necessitate attack from the most hindered *endo* face of the bicycle. All attempts to achieve this failed, however, so the hydration of **B** by *anti* addition of OH/H was considered next in order to set up the 4,5-*cis*/3,4-*trans* methyl/diol part (see **D**). This was also unsuccessful, so the epoxidation of **B** with a neutral agent, dimethyldioxirane, was examined, and, when successful, only one problem remained, that is, the opening of the highly strained epoxy-furoglycal **C** by clean S_N2 hydride attack from the least accessible *endo* face to provide the tetrahydrofurandiol **D**. Removal of the *trans*-diol from **D** to establish the olefin part in **A** was considered a minor problem owing to some precedent for this transformation in the literature (vide infra).

The required precursor of the nitrile oxide, the hydroximoyl chloride **8**,[21] was obtained from mannitol bis(acetonide) (**5**) by periodate cleavage, oximation, and subsequent chlorination (Scheme 2).[22–25] The nitrile oxide was generated in situ by the slow addition of triethylamine to a solution of **8** in methylfuran (Scheme 3), thus providing the low stationary-state concentration necessary for cycloaddition to such poorly reactive dipolarophiles.[17,26,27] The stereocentre at C-2 of the nitrile oxide, as expected, exhibited weak stereodifferentiation in the cycloaddition reaction, and so a mixture of diastereomers (60:40) was obtained, which were separated by MPLC to yield enantiomerically pure furoisoxazolines **9** and **10** in gram quantities in 40 and 27% yield, respectively. The major isomer **9** served for entry to the natural L-amino acid series **1**–**3** (with **10**, the D enantiomers of **2** and **3** were obtained[28]).

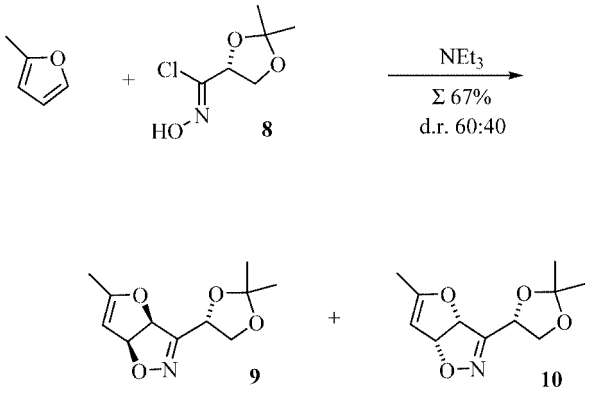
Epoxidation of the dihydrofuran **9** with dimethyldioxirane (DMDO)[29] led to the rather stable, isolable enol ether



Scheme 1. Retrosynthetic analysis of L-(+)-furanomycin **1**.

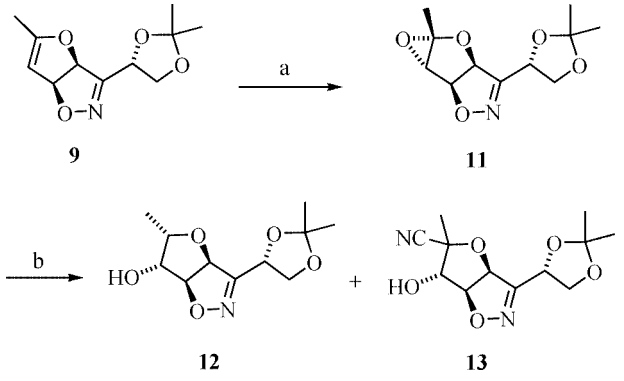


Scheme 2. Synthesis of the hydroximoyl chloride **8** from protected D-mannitol **5**. Reagents and conditions: a) $NaIO_4$; b) $HONH_2{\cdot}HCl$; c) *N*-chlorosuccinimide, DMF, HCl (cat.), room temp., 78% starting from **5**.



Scheme 3. Synthesis of diastereomeric furoisoxazolines **9** and **10** from 1,3-dipolar cycloaddition of **8** to 2-methylfuran. Reagents and conditions: 1.2 equiv. NEt_3, 2-methylfuran, 5 d, room temp., MPLC separation; yield: **9**, 40%; **10**, 27%.

epoxide **11**, a 1,2-anhydrofuranose derivative, in quantitative yield (Scheme 4). The epoxide could be stored for several days at low temperature (ca. –30 °C). The high selectivity of this reaction (*dr* > 95:5) can be rationalized in terms of the shape of the substrate; several examples are known that testify to the pronounced *exo* preference of attacks on this bicyclic system.[17–19]



Scheme 4. Epoxidation of furoisoxazoline **9** with dimethyldioxirane and reduction with sodium cyanoborohydride. Reagents and conditions: a) 2.0 equiv. Me_2CO_2 (0.1 M in acetone), CH_2Cl_2, 0 °C, 3 h, quant.; b) 2.0 equiv. $NaBH_3CN$–dioxane complex, 1.0 equiv. H_2O, THF, 16 h; **12** (74%) and **13** (5%) were obtained after MPLC separation.

Reductive opening of the epoxide **11** gave the alcohol **12** with the required 2,5-*trans* configuration at the tetrahydrofuran ring. The nucleophile (hydride) regio- and stereoselectively attacked the acetal carbon atom (C-5) in the enol ether epoxide **11** from the *endo* face of the bicyclic system (Figure 1). After screening several metal borohydride reagents,[30] it was found that the best results for epoxide opening were obtained with sodium cyanoborohydride in THF in the presence of one equivalent of water. A minor product, the cyanide adduct **13**, was also formed in this reaction (about 5%) and was removed by MPLC to give the required pure alcohol **12** in 74% yield.

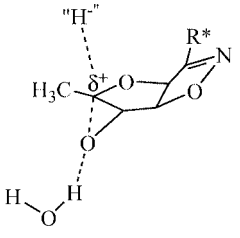
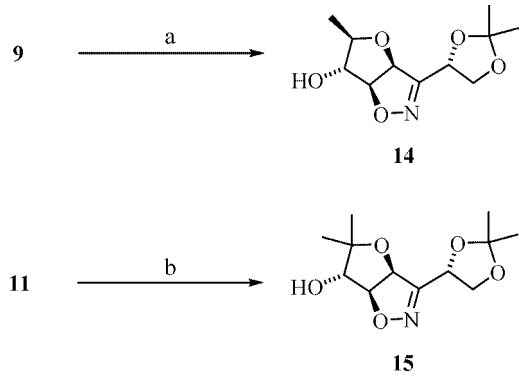


Figure 1. Proposed function of water in the reduction of the epoxide of **11** with $NaBH_3CN$.

The *endo* selectivity of the hydride addition in the epoxide-opening step is noteworthy. Water may act as a weak acid and thus activate the C-5 position towards a more "carbocation"-like transition state, resulting in an S_N2 course with inversion as is known from related reactions of simple epoxides. On the other hand, water could also protonate the alkoxide formed after epoxide opening thus reducing the tendency for polymerization (Figure 1).

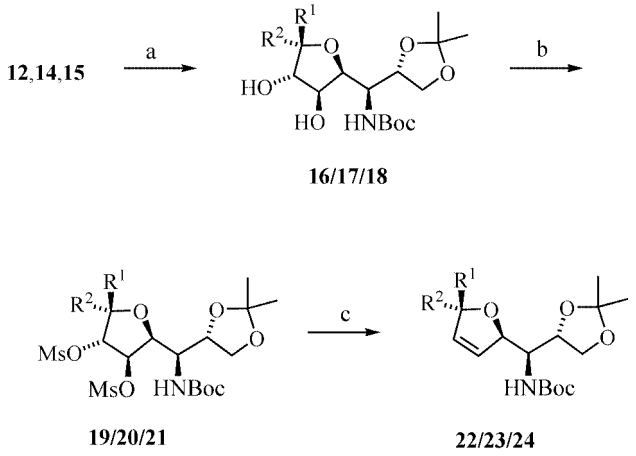
The 5-*epi* compounds (**14**, thence **2**) were accessed by hydration by means of a hydroboration/oxidation strategy. Reaction of the dihydrofuran **9** with borane–THF and subsequent oxidation with trimethylamine *N*-oxide dihydrate led to the alcohol **14** with high *exo* selectivity (*dr* > 9:1; Scheme 5). Similarly, the dimethyl compound **15** was obtained by regioselective opening of the epoxide **11** with methylmagnesium bromide, with a magnesium species presumably acting as the activating (Lewis) acid (Scheme 5).



Scheme 5. Hydroboration of the enol ether **9** and opening of the epoxide **11** with methylmagnesium bromide. Reagents and conditions: a) i. 2.0 equiv. BH_3·THF (1.0 M), THF, 0 °C, 7 h; ii. 7.0 equiv. $Me_3NO·2H_2O$, diglyme, 0→150 °C, 25 h; yield: **14**, 73%; b) 1.5 equiv. MeMgBr (3.0 M), THF, CH_2Cl_2, 15 min; yield: **15**, 83%.

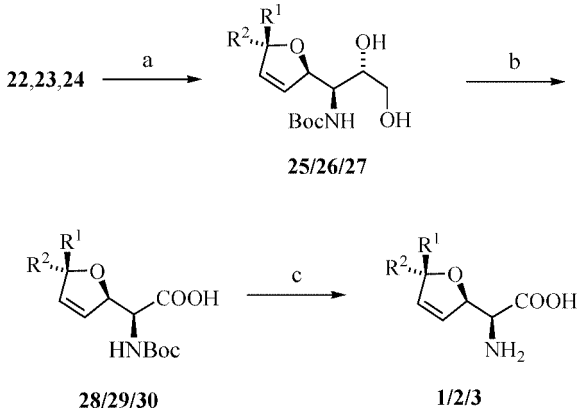
Next, the amino group in the side-chain and the C=C bond of the dihydrofuran ring had to be elaborated in order to obtain structures **22**–**24**. As expected from earlier work,[17–20] reduction of the isoxazolines **12**, **14**, and **15** with lithium aluminium hydride in THF/diethyl ether led to the corresponding 1,3-amino alcohols with high *exo* selectivity (>95:5 from NMR analyses). Hydride attack from the sterically less hindered *exo* side of the furoisoxazolines gave the *erythro*-1,3-amino alcohols. The free amino moiety was protected with Boc (in the absence of base) without touching the free OH groups to provide the *N*-Boc-amino diols **16**–**18** (Scheme 6). Introduction of the double bond was then effected by a di-*O*-(mesylation)/di-mesylate removal sequence. The diols **16**–**18** were first converted into the corresponding dimesylates **19**–**21**; in each case the stereochemical course of the preceding steps was verified by crystal structure analysis of **19**–**21**.[31–33] Next, treatment of the dimesylates **19**–**21** with sodium naphthalenide in THF[34,35] was considered, a mild elimination protocol that avoids high reaction temperatures. Indeed, this reaction readily afforded the di-deoxygenated 2,5-dihydrofurans **22**–**24** in 85, 81, and 75% yield, respectively.

Hydrolysis of the acetonide group with dilute trifluoroacetic acid (3–5%) proceeded without cleavage of the carbamate group to furnish the diols **25**–**27** in 88, 86, and 93% yield, respectively. Next, oxidative cleavage with sodium periodate provided the corresponding *N*-Boc-amino aldehydes which were immediately treated with buffered sodium chlorite. Racemization of *N*-Boc-amino aldehydes is often observed under strongly acidic or basic conditions.[36,37] However, mild oxidation in a weakly acidic medium led to



Scheme 6. Synthesis of the dihydrofuran intermediates **22**, **23**, and **24**. Reagents and conditions: a) i. 4.0 equiv. $LiAlH_4$, THF, diethyl ether, 0 °C→room temp., *dr* > 95:5; ii. 1.5–2.0 equiv. Boc_2O, dioxane/H_2O, 0 °C→room temp., 16 h; yield: **16**, 71%; **17**, 70%; **18**, 65%; b) 2.5 equiv. CH_3SO_2Cl, pyridine, 0 °C→room temp., 16 h; yield: **19**, 95%; **20**, 97%; **21**, 92%; c) sodium/naphthalene, THF, 0 °C, 15–30 min; yield: **22**, 85%; **23**, 75%; **24**, 81% [Boc = *tert*-butoxycarbonyl, Ms = methylsulfonyl (mesyl)].

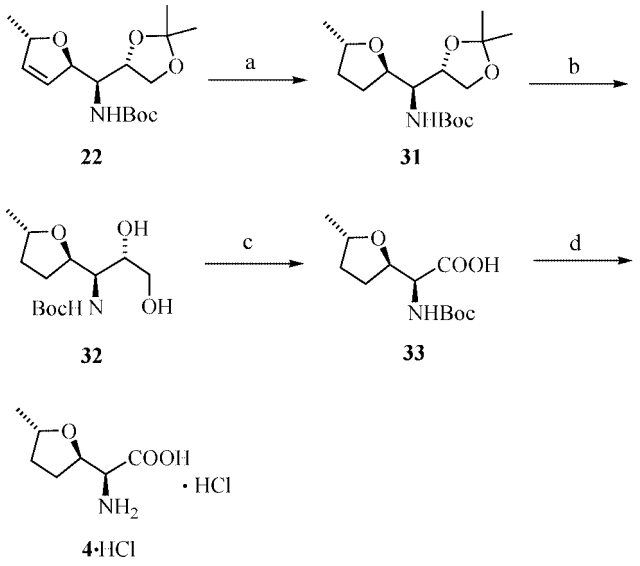
the optically pure, *N*-protected amino acids **28**–**30** (Scheme 7) in high yield. Finally, deprotection of *N*-Boc-furanomycin (**28**) with 6 N hydrochloric acid followed by ion-exchange chromatography and further purification by



Scheme 7. Synthesis of L-(+)-furanomycin (**1**), 5′-*epi*-furanomycin (**2**), and 5′-methylfuranomycin (**3**). Reagents and conditions: a) CF_3COOH/MeOH/H_2O, 0 °C→room temp., 18–30 h; yield: **25**, 88%; **26**, 86%; **27**, 86%; b) i. 1.2 equiv. $NaIO_4$, MeOH/H_2O, 1:1, 0 °C, 15–25 min; ii. 1.5–2.4 equiv. $NaClO_2$, 1.5–2.4 equiv. NaH_2PO_4, *t*BuOH, 2-methyl-2-butene, room temp., 2–3 h; yield: **28**, 89%; **29**, 93%; **30**, 93%; c) i. 6 N HCl, 4 °C or room temp., 2.5–16 h; ii. Dowex 50WX8 (H^+), 1 N NH_3; iii. recrystallization from H_2O/acetone or ethanol; yield: **1**, 61%; **2**, 60%; **3**, 56%.

crystallization from water/acetone provided L-(+)-furanomycin (**1**) in 61% yield [over-all yield of 6.3% starting from the commercially available mannitol bis(acetonide) (**5**)].

The dihydrofuranomycin (**4**) was obtained similarly.[38] First, the dihydrofuran derivative **22** was converted into the saturated tetrahydrofuran **31** in 80% yield by catalytic hydrogenation. Hydrolysis of the acetonide **31**, cleavage of the diol **32**, oxidation of the aldehyde, and deprotection of the amino group as above gave dihydrofuranomycin hydrochloride (**4**·HCl) in 29% yield in five steps from **22** (Scheme 8).



Scheme 8. Synthesis of L-(+)-dihydrofuranomycin (**4**) starting from the dihydrofuran derivative **22**. Reagents and conditions: a) H_2, Pd/C, MeOH; yield: **31**, 80%; b) CF_3COOH, MeOH/H_2O; yield: **32**, 77%; c) i. $NaIO_4$, *i*PrOH/H_2O, ii. 2.0 equiv. $NaClO_2$, 2.0 equiv. NaH_2PO_4, *t*BuOH, 2-methyl-2-butene, room temp., 16 h; yield: **33**, 75%; d) i. 4 N HCl, MeOH/H_2O; ii. Dowex 50WX8 (H^+); iii. conc. HCl; iv. recrystallization from H_2O/acetone; yield: **4**·HCl, 62%.

Biological Tests[39]

The growth–inhibitory activities of L-(+)-furanomycin (**1**) and its derivatives **2**, **3**, and **4** against several microorganisms were evaluated. Ampicillin was used as a reference antibiotic (Table 1). From these experiments, several aspects of the structure–activity relationship were determined. As reported in the literature,[3] L-(+)-furanomycin (**1**) showed a minimal inhibitory concentration (MIC) of 4 μg mL^{-1} against two *E. coli* strains and 2 μg mL^{-1} and 4 μg mL^{-1} against two *S. aureus* strains, respectively. 5′-*epi*-Furanomycin (**2**) and the 5′-methyl derivative **3** showed no activity against the bacteria tested. Thus, the configuration at C-5′ seems to be essential for biological activity, while the β-methyl group at C-5′ (as in **2** and **3**) seems rather detrimental. L-Dihydrofuranomycin (**4**) showed very weak activity against Gram-positive *S. aureus* (32–64 μg mL^{-1}) and no activity against the other Gram-negative bacteria.

Table 1. Growth inhibition of bacterial strains by L-(+)-furanomycin (**1**), 5′-*epi*-furanomycin (**2**), 5′-methylfuranomycin (**3**), and L-(+)-dihydrofuranomycin (**4**) (MIC [$\mu g\,mL^{-1}$]).

Bacterial strain	MIC [$\mu g\,mL^{-1}$]				
	1	**2**	**3**	**4**	Ampicillin
Staphylococcus aureus 133	2	>32	>32	32–64	0.25
Staphylococcus aureus 44	4	>32	>32	32–64	2
Proteus vulgaris 1017	>32	>32	>32	>32	>32
Klebsiella pneumoniae 8085	>32	>32	>32	>32	>32
E. coli Neumann	4	>32	>32	>32	4
E. coli A 261	4	>32	>32	>32	>32

Conclusions

The results of these studies offer a practical and stereoselective approach to gram quantities of L-(+)-furanomycin (**1**) through 1,3-dipolar cycloaddition of a nitrile oxide to methylfuran in 14 steps [from the commercially available mannitol bis(acetonide)] with an overall yield of 6.3%. Glyceronitrile oxide served as a chiral glycine equivalent. The cycloaddition products, the furoisoxazolines **9**, bear three stereocentres from which the target structure L-(+)-furanomycin (**1**), and the 5′-epimer (**2**), 5′-methylfuranomycin (**3**), and L-(+)-dihydrofuranomycin (**4**) were derived following highly stereoselective operations. Starting from the furoisoxazoline **10**, the enantiomers of **2** and **3** (D stereoisomers) were obtained using the same protocol.[28] In addition, structural analogues of **1** can now be synthesized since various other groups can be introduced by nucleophilic addition to the epoxide **11**.[28]

Experimental Section

General Remarks: Melting points were determined on a Fisher–Johns 4017 heating block and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on Bruker AC 250, ARX 300, and ARX 500 spectrometers using Me_4Si as the internal standard. IR spectra were recorded on a Perkin–Elmer 283 or Bruker IFS 28 IR spectrometer. Mass spectra and high-resolution mass spectra (HRMS) were obtained with Finnigan quadrupole-MS 4500 and Finnigan MAT 95 spectrometers, respectively. Optical rotations were determined with a Perkin–Elmer 241 MC polarimeter. MPLC separations were carried out using a Lewa FL 1 pump and products were detected with a Knauer 97.00 diode array detector or a Knauer differential refractometer. The columns (4 cm × 40 cm, N = 11600, pressure = 10–15 bar, flow rate = 40–60 $mL\,min^{-1}$) were packed with LiChroprep Si 60 silica gel (size 15–25 μm).[40]

Solvents were purified and dried using standard methods. Silica gel (40–63 mL, E. Merck) was used in column chromatography and acidic resin Dowex 50WX8 (H^+ form, Fluka) in ion-exchange purification.

(3a*S*,6a*S*,1′*S*)- and (3a*R*,6a*R*,1′*S*)-3-(1′,2′-*O*-Isopropylidenedioxyethyl)-5-methyl-3a,6a-dihydrofuro[2,3-*d*]isoxazole (9 and 10): 2.0 M Triethylamine solution (36.5 mL, 73.0 mmol) in 2-methylfuran was added very slowly (0.01 $mL\,min^{-1}$) to a stirred solution of the (*R*)-hydroximoyl chloride **8**[21–25] (10.9 g, ca. 92% purity, 60.7 mmol) in freshly distilled 2-methylfuran (300 mL) using a motor-driven syringe. After addition of water (50 mL) and separation of the phases, the organic layer was washed with water (50 mL), dried ($MgSO_4$), and filtered. The solvent was evaporated in vacuo and the residue was filtered through a pad of silica gel. The remaining orange-coloured oil was separated by MPLC (eluent: petroleum ether/ethyl acetate, 4:1) to afford the furoisoxazolines **9** (*anti*, 5.40 g, 40%) and **10** (*syn*, 3.63 g, 27%) as colourless oils. Furoisoxazoline **9** (*anti*): $[\alpha]_D^{20}$ = –171 (*c* = 1.48, $CHCl_3$). IR (film): $\tilde{\nu}$ = 2990, 2935, 1665, 1380, 1340, 1220, 1155, 1065, 1030, 940, 910, 850 cm^{-1}. ^1H NMR (500.1 MHz, $CDCl_3$): δ = 1.44, 1.45 [2 s, 6 H, $C(CH_3)_2$], 1.89 (s, 3 H, 5-CH_3), 4.28 (dd, $J_{1',2'A}$ = 6.5, $J_{2'A,2'B}$ = 8.6 Hz, 1 H, 2′-H_A), 4.31 (dd, $J_{1',2'B}$ = 5.9, $J_{2'A,2'B}$ = 8.6 Hz, 1 H, 2′-H_B), 4.91 ("t", $J_{1',2'A}$ = $J_{1',2'B}$ = 6.2 Hz, 1 H, 1′-H), 4.97 (dq, $J_{6,6a}$ = 2.5, $J_{6,Me}$ = 1.2 Hz, 1 H, 6-H), 5.80 (ddq, $J_{3a,6a}$ = 8.6, $J_{6,6a}$ = 2.5, $J_{6a,Me}$ = 1.2 Hz, 1 H, 6a-H), 5.88 (d, $J_{3a,6a}$ = 8.6 Hz, 1 H, 3a-H) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 13.4 (5-CH_3), 25.5, 26.3 [$C(CH_3)_2$], 67.0 (C-2′), 70.4 (C-1′), 88.8, 88.9 (C-3a, C-6a), 96.8 (C-6), 110.4 [$C(CH_3)_2$], 154.8 (C-3), 159.8 (C-5) ppm. $C_{11}H_{15}NO_4$ (225.2): calcd. C 58.66, H 6.71, N 6.22; found C 58.82, H 6.79, N 6.25. Furoisoxazoline **10** (*syn*): $[\alpha]_D^{20}$ = +199 (*c* = 1.52, $CHCl_3$). IR (film): $\tilde{\nu}$ = 2990, 1665, 1385, 1250, 1215, 1065, 1030, 850 cm^{-1}. ^1H NMR (500.1 MHz, $CDCl_3$): δ = 1.45, 1.52 [2 s, 6 H, $C(CH_3)_2$], 1.88 (s, 3 H, 5-CH_3), 4.16 (dd, $J_{1',2'A}$ = 7.1, $J_{2'A,2'B}$ = 8.6 Hz, 1 H, 2′-H_A), 4.18 (dd, $J_{1',2'B}$ = 6.8, $J_{2'A,2'B}$ = 8.6 Hz, 1 H, 2′-H_B), 4.99 (dq, $J_{6,6a}$ = 2.5, $J_{6,Me}$ = 1.2 Hz, 1 H, 6-H), 5.08 ("t", $J_{1',2'A}$ = $J_{1',2'B}$ = 7.0 Hz, 1 H, 1′-H), 5.80 (ddq, $J_{3a,6a}$ = 8.7, $J_{6,6a}$ = 2.5, $J_{6a,Me}$ = 1.2 Hz, 1 H, 6a-H), 5.92 (d, $J_{3a,6a}$ = 8.7 Hz, 1 H, 3a-H) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 13.4 (5-CH_3), 25.6, 26.1 [$C(CH_3)_2$], 66.7 (C-2′), 71.0 (C-1′), 87.8, 89.5 (C-3a, C-6a), 96.7 (C-6), 110.4 [$C(CH_3)_2$], 153.9 (C-3), 159.8 (C-5) ppm. $C_{11}H_{15}NO_4$ (225.2): calcd. C 58.66, H 6.71, N 6.22; found C 58.82, H 6.79, N 6.25.

(3a*S*,5*S*,6*S*,6a*R*,1′*S*)-5,6-Epoxy-3-(1′,2′-*O*-isopropylidenedioxyethyl)-5-methyl-3a,5,6,6a-tetrahydrofuro[2,3-*d*]isoxazole (11): Dimethyldioxirane solution in acetone (ca. 1 mmol, ca. 0.1 M, 10 mL) was added to a stirred solution of the isoxazoline **9** (90 mg, 0.40 mmol) in dry CH_2Cl_2 (2 mL) at 0 °C.[29] The mixture was stirred at 0 °C for 3 h. The solvent was evaporated in vacuo (ice bath, 10 mbar), the residue was dissolved in dry CH_2Cl_2 (ca. 5 mL), and re-evaporated in order to remove residual solvent as an azeotrope; this was repeated twice. After drying in vacuo (0.05 mbar), the epoxide **11** was obtained as a colourless, analytically pure solid, m.p. 31–33 °C. $[\alpha]_D^{20}$ = –191 (*c* = 1.02, $CHCl_3$). IR (film): $\tilde{\nu}$ = 2987, 1480, 1460, 1374, 1247, 1199, 1152, 1060, 906, 865, 842, 809 cm^{-1}. ^1H NMR (300.1 MHz, $CDCl_3$): δ = 1.41, 1.43 [2 s, 6 H, $C(CH_3)_2$], 1.72 (s, 3 H, 5-CH_3), 3.73 (s, 1 H, 6-H), 4.20 (dd, $J_{1',2'A}$ = 5.7, $J_{2'A,2'B}$ = 8.6 Hz, 1 H, 2′-H_A), 4.26 (dd, $J_{1',2'B}$ = 6.4, $J_{2'A,2'B}$ = 8.6 Hz, 1 H, 2′-H_B), 4.93 ("t", $J_{1',2'A}$ = $J_{1',2'B}$ = 6.1 Hz, 1 H, 1′-H), 5.28, 5.32 (2 d, $J_{3a,6a}$ = 7.5 Hz, 2 H, 3a-H, 6a-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 15.8 (5-CH_3), 25.6, 25.8 [$C(CH_3)_2$], 62.5 (C-6), 67.5 (C-2′), 70.1 (C-1′), 84.3, 89.2 (C-3a, C-6a), 90.9 (C-5), 110.9 [$C(CH_3)_2$], 156.8 (C-3) ppm. $C_{11}H_{15}NO_5$ (241.2): calcd. C 54.76, H 6.27, N 5.81; found C 54.84, H 6.29, N 5.68.

(3a*S*,5*S*,6*R*,6a*R*,1′*S*)-6-Hydroxy-3-(1′,2′-*O*-isopropylidenedioxyethyl)-5-methyl-3a,5,6,6a-tetrahydrofuro[2,3-*d*]isoxazole (12) and (3a*S*,6*R*,6a*R*,1′*S*)-5-Cyano-6-hydroxy-3-(1′,2′-*O*-isopropylidenedioxyethyl)-5-methyl-3a,5,6,6a-tetrahydrofuro[2,3-*d*]isoxazole (13): A solution of sodium cyanoborohydride–dioxane complex[41] (478 mg, 2.0 mmol) in dry THF (2 mL) and water (ca. 20 μL, 1.1 mmol) was cooled to 0 °C and a solution of the epoxide **11** (241 mg, 0.99 mmol) in dry THF was added dropwise within 5 min. The cooling bath was removed and the reaction mixture was stirred at room temp. for 16 h. After addition of a saturated aqueous solution of NH_4Cl (10 mL) and water (30 mL) the reaction mixture was extracted with CH_2Cl_2 (five times, 80 mL total). The combined organic phases were dried ($MgSO_4$), filtered, and the solvent evaporated to leave a colourless oil, which contained compounds **12** and **13** (96:4 according to ^{13}C NMR). After flash chromatography (10 cm × 2 cm, petroleum ether/ethyl acetate, 1:1), both compounds were separated by MPLC (petroleum ether/ethyl acetate, 1:1) to give **12** as a colourless oil (181 mg, 74%) and cyanide **13** (8 mg, 5%). Compound **12**: $[\alpha]_D^{20} = -32.7$ (c = 1.55, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3453 (bs), 2987, 2938, 1456, 1219, 1152, 1118, 1067, 981, 841 cm^{-1}. ^1H NMR (300.1 MHz, $CDCl_3$): δ = 1.32 (d, $J_{5,Me}$ = 6.5 Hz, 3 H, 5-CH_3), 1.42, 1.44 [2 s, 6 H, $C(CH_3)_2$], 2.73 (br. s, 1 H, OH), 3.61 (dq, $J_{5,Me}$ = 6.5, $J_{5,6}$ = 2.7 Hz, 1 H, 5-H), 4.10 (d, $J_{5,6}$ = 2.7 Hz, 1 H, 6-H), 4.20 (dd, $J_{1',2'A}$ = 5.9, $J_{2'A,2'B}$ = 8.6 Hz, 1 H, 2′-H_A), 4.26 (dd, $J_{1',2'B}$ = 6.4, $J_{1'A,1'B}$ = 8.6 Hz, 1 H, 2′-H_B), 4.86 (d, $J_{3a,6a}$ = 6.9 Hz, 1 H, 6a-H), 4.91 (d"t", $J_{3a,1'}$ = 0.6, $J_{1',2'A}$ = $J_{1',2'B}$ = 6.2 Hz, 1 H, 1′-H), 5.61 (d, $J_{3a,6a}$ = 6.9 Hz, 1 H, 3a-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 12.3 (5-CH_3), 25.5, 26.2 [$C(CH_3)_2$], 67.0 (C-2′), 70.0 (C-1′), 75.8 (C-5), 76.5 (C-6), 86.4 (C-3a), 88.8 (C-6a), 110.4 [$C(CH_3)_2$], 156.1 (C-3) ppm. $C_{11}H_{17}NO_5$ (243.3): calcd. C 54.31, H 7.04, N 5.76; found C 54.27, H 7.18, N 5.78. Cyanide **13**: ^1H NMR (300.1 MHz, $CDCl_3$): δ = 1.44, 1.45, 1.68 [3 s, 9 H, 5-CH_3, $C(CH_3)_2$], 3.65 (br. s, 1 H, OH), 4.28 (dd, $J_{1',2'A}$ = 5.7, $J_{2'A,2'B}$ = 8.7 Hz, 1 H, 2′-H_A), 4.32 (dd, $J_{1',2'B}$ = 6.3, $J_{2'A,2'B}$ = 8.7 Hz, 1 H, 2′-H_B), 4.63 (br. s, 1 H, 6-H), 5.00 ("t", $J_{1',2'A}$ = $J_{1',2'B}$ = 6.0 Hz, 1 H, 1′-H), 5.02 (d, $J_{3a,6a}$ = 7.1 Hz, 1 H, 6a-H), 5.73 (d, $J_{3a,6a}$ = 7.1 Hz, 1 H, 3a-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.0 (5-CH_3), 25.4, 26.2 [$C(CH_3)_2$], 67.2 (C-2′), 70.0 (C-1′), 78.2 (C-5), 79.7, 88.1, 89.4 (C-3a, C-6, C-6a), 110.7 [$C(CH_3)_2$], 119.2 (CN), 156.9 (C-3) ppm.

(2*S*,3*R*,4*R*,5*S*,1′*R*,2′*S*)-2-(1′-*tert*-Butoxycarbonylamino-2′,3′-*O*-isopropylidenedioxypropyl)-3,4-dihydroxy-5-methyltetrahydrofuran (16): In accord with the procedure given in ref.[42] $LiAlH_4$ (104 mg, 2.7 mmol) was suspended under nitrogen in dry diethyl ether (2 mL) in a flame-dried flask. The mixture was cooled to 0 °C and **12** (166 mg, 0.68 mmol) in dry THF (2 mL) was added dropwise. The ice bath was removed and the reaction mixture was stirred at room temp. for 16 h. According to ref.[43] the reaction mixture was then hydrolysed with water (0.15 mL), a 20% aqueous solution of NaOH (0.1 mL), and water (0.5 mL) whilst stirring for 3 h. After addition of $MgSO_4$ (2 g) and stirring for 5 h at room temp., the mixture was filtered and the filter cake was washed thoroughly with CH_2Cl_2 (200 mL). After evaporation of the solvent, a colourless oil was obtained, which was dissolved in dioxane/water (3:1, 4 mL). Di-*tert*-butyl dicarbonate (279 mg, 1.22 mmol) was then added at 0 °C. The cooling bath was removed and the reaction mixture was stirred at room temp. for 16 h. After addition of water (30 mL) the mixture was extracted with CH_2Cl_2 (4 × 20 mL), and dried ($MgSO_4$). After concentration of the solvent, the residue was purified by flash chromatography (20 cm × 2 cm, petroleum ether/ethyl acetate, 4:6) to afford the amino alcohol **16** as a colourless solid (167 mg, 71%), m.p. 116–118 °C. $[\alpha]_D^{20}$ = +30.9 (c = 1.50, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3451 (bs), 2983, 1713, 1500, 1369, 1173, 1060 cm^{-1}. ^1H NMR (300.1 MHz, CD_3OD, 328 K): δ = 1.19 (d, $J_{5,Me}$ = 6.5 Hz, 3 H, 5-CH_3), 1.33, 1.39 [2 s, 6 H, $C(CH_3)_2$], 1.44 [s, 9 H, $C(CH_3)_3$], 3.88 (dd, $J_{2',3'A}$ = 6.6, $J_{3'A,3'B}$ = 8.4 Hz, 1 H, 3′-H_A), 3.92 and 4.11 (2 m_c, 5 H, 1′-H, 2′-H, 2-H, 3-H, 4-H), 4.02 (dd, $J_{2',3'B}$ = 6.2, $J_{3'A,3'B}$ = 8.4 Hz, 1 H, 3′-H_B), 4.24 (dq, $J_{4,5}$ = 3.6, $J_{5,Me}$ = 6.5 Hz, 1 H, 5-H) ppm. ^{13}C NMR (75.5 MHz, CD_3OD, 328 K): δ = 15.2 (5-CH_3), 26.5, 27.6 [$C(CH_3)_2$], 29.6 [$C(CH_3)_3$], 54.4 (C-1′), 68.6 (C-3′), 78.3 (C-5), 78.4, 80.1, 80.3, 80.5 (C-2, C-3, C-4, C-2′), 81.1 [$C(CH_3)_3$], 111.4 [$C(CH_3)_2$], 158.9 (C=O) ppm. $C_{16}H_{29}NO_7$ (347.4): calcd. C 55.32, H 8.41, N 4.03; found C 55.11, H 8.44, N 4.00.

(2*S*,3*R*,4*R*,5*S*,1′*R*,2′*S*)-2-(1′-*tert*-Butoxycarbonylamino-2′,3′-*O*-isopropylidenedioxypropyl)-5-methyl-3,4-bis(methylsulfonyloxy)tetrahydrofuran (19): Mesyl chloride (240 μL, 3.10 mmol) was added to a stirred solution of the *N*-Boc-amino alcohol **16** (430 mg, 1.24 mmol) in dry pyridine (3 mL) at 0 °C; the mixture was allowed to warm to room temp. over night. The mixture was then poured onto crushed ice (20 mL), extracted with CH_2Cl_2 (five times, 80 mL total), and dried ($MgSO_4$). After concentration of the solvent, the residue was purified by flash chromatography (12 cm × 2.5 cm, petroleum ether/ethyl acetate, 1:1) to afford the dimesylate **19** (595 mg, 95%) as a colourless foam, which was recrystallized from heptane/ethyl acetate, m.p. 88–89 °C. A crystal structure analysis of this material was performed.[31] $[\alpha]_D^{20}$ = –4.2 (c = 1.50, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3357, 2986, 1740, 1707, 1521, 1367, 1239, 1170, 1144, 963, 890, 856 cm^{-1}. ^1H NMR (500.1 MHz, C_6D_6): δ = 1.40 (d, $J_{5,Me}$ = 6.5 Hz, 3 H, 5-CH_3), 1.58, 1.75 [2 s, 6 H, $C(CH_3)_2$], 1.76 [s, 9 H, $C(CH_3)_3$], 2.75, 2.95 (2 s, 6 H, 2 H_3CSO_3), 4.20 (dq, $J_{4,5}$ = 3.8, $J_{5,Me}$ = 6.5 Hz, 1 H, 5-H), 4.21, 4.36 (2 m, 4 H, 1′-H, 2′-H, 3′-H_A, 3′-H_B), 4.99 (dd, $J_{2,3}$ = 5.0, $J_{2,1'}$ = 0.7 Hz, 1 H, 2-H), 5.14 (d, $J_{1',NH}$ = 9.8 Hz, 1 H, NH), 5.19 (dd, $J_{2,3}$ = 5.0, $J_{3,4}$ = 1.9 Hz, 1 H, 3-H), 5.36 (dd, $J_{3,4}$ = 1.9, $J_{4,5}$ = 3.8 Hz, 1 H, 4-H) ppm. ^{13}C NMR (125.8 MHz, C_6D_6): δ = 15.0 (5-CH_3), 25.8, 27.3 [$C(CH_3)_2$], 28.8 [$C(CH_3)_3$], 37.4, 37.9 (H_3CSO_3), 52.2 (C-1′), 67.7 (C-3′), 76.2 (C-2), 76.4 (C-5), 76.9 (C-2′), 80.2 [$C(CH_3)_3$], 83.6 (C-3), 84.7 (C-4), 110.5 [$C(CH_3)_2$], 156.1 (C=O) ppm. $C_{18}H_{33}NO_{11}S_2$ (503.6): calcd. C 42.93, H 6.61, N 2.78, S 12.73; found C 42.90, H 6.53, N 2.71, S 12.64.

(2*R*,5*S*,1′*S*,2′*S*)-2-(1′-*tert*-Butoxycarbonylamino-2′,3′-*O*-isopropylidenedioxypropyl)-5-methyl-2,5-dihydrofuran (22): In accord with the procedure described in ref.[35], sodium (280 mg, 12.2 mmol) and naphthalene (1.56 g, 12 mmol) were dissolved in dry THF (12 mL) under nitrogen and stirred for 3 h at room temp. A portion (8 mL) of this solution was then transferred to another round-bottomed flask by syringe, and a solution of the dimesylate **19** (895 mg, 1.78 mmol) in dry THF (3 mL) was added dropwise under nitrogen at 0 °C. After stirring for 20 min, the reaction was quenched with methanol (1 mL) and water (1 mL). Stirring was continued for 10 min and then a saturated aqueous solution of NH_4Cl was added. The reaction mixture was extracted with CH_2Cl_2 (five times, 80 mL total) and dried ($MgSO_4$). After evaporation of the solvent, the residue was purified by flash chromatography (10 cm × 2.5 cm, petroleum ether/ethyl acetate, 4:1) to afford **22** (474 mg, 85%) as a colourless solid, m.p. 89–90 °C. $[\alpha]_D^{20}$ = +194 (c = 1.32, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3370, 3332, 2987, 1686, 1519, 1368, 1288, 1168, 1080, 1063, 1049 cm^{-1}. ^1H NMR (300.1 MHz, $CDCl_3$, 323 K): δ = 1.24 (d, $J_{5,Me}$ = 6.3 Hz, 3 H, 5-CH_3), 1.35, 1.41 [2 s, 15 H, $C(CH_3)_2$, $C(CH_3)_3$], 3.70 (br. m, 1 H, 1′-H), 3.87 (dd, $J_{2',3'A}$ = 5.5, $J_{3'A,3'B}$ = 8.1 Hz, 1 H, 3′-H_A), 4.04 (dd, $J_{2',3'B}$ = 6.2, $J_{3'A,3'B}$ = 8.1 Hz, 1 H, 3′-H_B), 4.09 (m_c, 1 H, 2′-H), 4.47 (br. s, 1 H, NH), 4.95 (dddq, $J_{2,5}$ = 5.8, $J_{3,5}$ = 2.1, $J_{4,5}$ = 1.5, $J_{5,Me}$ = 6.3 Hz, 1 H, 5-H), 5.16 (dd"t", $J_{2,3}$ = $J_{2,1'}$ = 1.5, $J_{2,4}$ = 2.3, $J_{2,5}$ = 5.8 Hz, 1 H, 2-H), 5.69 (br. d"t", $J_{2,3}$ = $J_{3,5}$ = 1.8, $J_{3,4}$ = 6.1 Hz, 1 H, 3-H), 5.84 (ddd, $J_{2,4}$ = 2.3, $J_{3,4}$

= 6.1, $J_{4,5}$ = 1.5 Hz, 1 H, 4-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$, 323 K): δ = 22.0 (5-CH_3), 25.6, 26.9 [$C(CH_3)_2$], 28.4 [$C(CH_3)_3$], 56.3 (C-1′), 67.7 (C-3′), 75.9 (C-2′), 79.5 [$C(CH_3)_3$], 83.1 (C-5), 84.6 (C-2), 109.7 [$C(CH_3)_2$], 127.1 (C-3), 133.0 (C-4), 159.0 (C=O) ppm. $C_{16}H_{27}NO_5$ (313.4): calcd. C 61.32, H 8.68, N 4.47; found C 61.54, H 8.64, N 4.44.

(2*R*,5*S*,1′*S*,2′*S*)-2-(1′-*tert*-Butoxycarbonylamino-2′,3′-dihydroxypropyl)-5-methyl-2,5-dihydrofuran (25): A solution of **22** (370 mg, 1.18 mmol) in methanol (4 mL) and water (1 mL) was treated with trifluoroacetic acid (0.15 mL) and allowed to stand for 18 h. After neutralisation with aqueous ammonia (1 N, 4 mL), silica gel (0.5 g) was added to the mixture and the solvent was evaporated. The silica gel with the adsorbed product was loaded onto the top of a column of silica gel and purified by flash chromatography (15 cm × 2 cm, petroleum ether/ethyl acetate, 4:6) to afford the diol **25** as a colourless wax (285 mg, 88%). $[\alpha]_D^{20}$ = +190 (*c* = 1.34, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3359, 1693, 1249, 1173, 1087, 1060 cm^{-1}. ^{1}H NMR (300.1 MHz, CD_3OD, 333 K): δ = 1.22 (d, $J_{5,Me}$ = 6.3 Hz, 3 H, 5-CH_3), 1.42 [s, $C(CH_3)_3$], 3.55, 3.66, 3.69 (3 m, 3 H, 2′-H, 3′-H_A, 3′-H_B), 3.60 (m_c, $J_{2,1'}$ = 1.6 Hz, 1 H, 1′-H), 4.98 (dddq, $J_{2,5}$ = 5.7, $J_{3,5}$ = 2.1, $J_{4,5}$ = 1.5, $J_{5,Me}$ = 6.3 Hz, 1 H, 5-H), 5.25 (dd"t", $J_{2,3}$ = $J_{2,1'}$ = 1.6, $J_{2,4}$ = 2.3, $J_{2,5}$ = 5.7 Hz, 1 H, 2-H), 5.72 (ddd, $J_{2,3}$ = 1.6, $J_{3,4}$ = 6.2, $J_{3,5}$ = 2.1 Hz, 1 H, 3-H), 5.88 (ddd, $J_{2,4}$ = 2.3, $J_{3,4}$ = 6.2, $J_{4,5}$ = 1.5 Hz, 1 H, 4-H) ppm. ^{13}C NMR (75.5 MHz, CD_3OD, 333 K): δ = 22.8 (5-CH_3), 29.4 [$C(CH_3)_3$], 57.0 (C-1′), 65.8 (C-3′), 73.9 (C-2′), 81.1 [$C(CH_3)_3$], 84.7 (C-5), 86.3 (C-2), 128.9 (C-3), 134.4 (C-4), 159.0 (C=O) ppm. $C_{13}H_{23}NO_5$ (273.3): calcd. C 57.13, H 8.48, N 5.12; found C 56.90, H 8.42, N 4.98.

(2*S*,2′*R*,5′*S*)-2-(*tert*-Butoxycarbonylamino)-2-(5′-methyl-2′,5′-dihydrofuran-2′-yl)acetic Acid (28): Sodium metaperiodate (178 mg, 0.83 mmol) was added to a stirred solution of the diol **25** (190 mg, 0.70 mmol) in methanol (2 mL) and water (2 mL) was added at 0 °C. After 25 min, TLC indicated that the reaction had gone to completion. Water (15 mL) was then added, and the reaction mixture was extracted with CH_2Cl_2 (five times, 70 mL in total) and dried ($MgSO_4$). The solvent was evaporated at 0 °C to give the aldehyde as a colourless oil. In accord with the procedure given in ref.[44–47], this was dissolved in *tert*-butyl alcohol (5 mL) and 2-methyl-2-butene (2 mL) and then treated with a solution of $NaClO_2$ (150 mg, 1.67 mmol) and NaH_2PO_4 (200 mg, 1.67 mmol) in water (1.5 mL) over a period of 3 h. After addition of a 20% aqueous solution of NaOH (0.5 mL) the solvent was evaporated. The residue was dissolved in water (30 mL) and washed three times with diethyl ether (45 mL total). The aqueous phase was acidified with dilute sulfuric acid (pH 2–3) and extracted with diethyl ether. The organic layer was washed with a saturated solution of sodium thiosulfate (10 mL) and dried ($MgSO_4$). The solvent was evaporated to give pure *N*-Boc-amino acid **28** (159 mg, 89%) as a colourless solid, m.p. 151–153 °C. $[\alpha]_D^{20}$ = +182 (*c* = 1.49, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3449, 2973, 1737, 1665, 1524, 1406, 1372, 1354, 1251 cm^{-1}. ^{1}H NMR (300.1 MHz, $CDCl_3$, 323 K): δ = 1.24 (d, $J_{5',Me}$ = 6.4 Hz, 3 H, 5′-CH_3), 1.43 [s, $C(CH_3)_3$], 4.45 (br. s, 1 H, 2-H), 5.04 (dddq, $J_{2',5'}$ = 5.6, $J_{3',5'}$ = 1.6, $J_{4',5'}$ = 1.4, $J_{5',Me}$ = 6.4 Hz, 1 H, 5′-H), 5.16 (br. s, 1 H, NH), 5.37 (dd"t", $J_{2,2'}$ = $J_{2',4'}$ = 2.2, $J_{2',3'}$ = 1.6, $J_{2',5'}$ = 5.6 Hz, 1 H, 2′-H), 5.76 (d"t", $J_{2',3'}$ = $J_{3',5'}$ = 1.6, $J_{3',4'}$ = 6.2 Hz, 1 H, 3′-H), 5.91 (ddd, $J_{2',4'}$ = 2.2, $J_{3',4'}$ = 6.2, $J_{4',5'}$ = 1.5 Hz, 1 H, 4′-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$, 323 K): δ = 21.6 (5′-CH_3), 28.3 [$C(CH_3)_3$], 56.7 (C-2), 80.1 [$C(CH_3)_3$], 83.6 (C-5′), 86.2 (C-2′), 125.6 (C-3′), 133.7 (C-4′), 155.9 (C=O), 174.6 (C-1) ppm. $C_{12}H_{19}NO_5$ (257.3): calcd. C 56.02, H 7.44, N 5.44; found C 55.61, H 7.37, N 5.24.

(2*S*,2′*R*,5′*S*)-2-Amino-2-(5′-methyl-2′,5′-dihydrofuran-2′-yl)acetic Acid, L-(+)-Furanomycin (1): Conc. HCl (4 mL) was added to a stirred solution of the *N*-Boc-amino acid **28** (259 mg, 1.01 mmol) in methanol and water (1:1, 4 mL). After standing for 16 h in the cold (4 °C), the solvent was removed. The residue was purified by means of an ion-exchange column (Dowex 50WX8, H^+ form), which, after elution with 1 N aqueous ammonia, gave the crude product as an orange-coloured solid. After recrystallization from water and acetone, pure furanomycin **1** was obtained as a colourless solid (97 mg, 61%), m.p. 221–224 °C; lit.[3]: 220–223 °C. $[\alpha]_D^{20}$ = +144 (*c* = 1.00, H_2O); lit.[3]: +136.1 (*c* = 1.0, H_2O). IR (KBr): $\tilde{\nu}$ = 3480, 3137, 2963, 1632, 1568, 1523, 1401, 1384, 1349, 1088, 1054, 1019, 730 cm^{-1}. ^{1}H NMR (500.1 MHz, D_2O): δ = 1.14 (d, $J_{5',Me}$ = 6.4 Hz, 3 H, 5′-CH_3), 3.75 (d, $J_{2,2'}$ = 2.6 Hz, 1 H, 2-H), 5.00 (dddq, $J_{2',5'}$ = 5.6, $J_{3',5'}$ = 2.2, $J_{4',5'}$ = 1.5, $J_{5',Me}$ = 6.4 Hz, 1 H, 5′-H), 5.34 (dddd, $J_{2,2'}$ = 2.6, $J_{2',3'}$ = 1.6, $J_{2',4'}$ = 2.3, $J_{2',5'}$ = 5.6 Hz, 1 H, 2′-H), 5.74 (ddd, $J_{2',3'}$ = 1.6, $J_{3',4'}$ = 6.2, $J_{3',5'}$ = 2.2 Hz, 1 H, 3′-H), 6.07 (ddd, $J_{2',4'}$ = 2.3, $J_{3',4'}$ = 6.2, $J_{4',5'}$ = 1.5 Hz, 1 H, 4′-H) ppm. ^{13}C NMR (125.8 MHz, D_2O): δ = 21.0 (5′-CH_3), 57.4 (C-2), 84.2, 84.3 (C-2′, C-5′), 124.3 (C-3′), 136.2 (C-4′), 172.3 (C-1) ppm. $C_7H_{11}NO_3$ (157.2): calcd. C 53.50, H 7.05, N 8.91; found C 53.21, H 7.01, N 8.75. MS (FAB pos., glycerol, 325 K): *m/z* (%) = 158 (100) $[M + H]^+$, 315 (30) $[2M + H]^+$. HRMS (FAB pos.): $C_7H_{12}NO_3$, $[M + H]^+$: calcd. 158.0817; found 158.0815.

(3a*S*,5*R*,6*R*,6a*R*,1′*S*)-6-Hydroxy-3-(1′,2′-*O*-isopropylidenedioxyethyl)-5-methyl-3a,5,6,6a-tetrahydrofuro[2,3-*d*]isoxazole (14): In a flame-dried flask, isoxazoline **9** (450 mg, 2 mmol) was dissolved in THF (7 mL) under nitrogen. The mixture was cooled to 0 °C and a solution of BH_3·THF (1 M, 2.5 mL, 2.5 mmol) was added dropwise over a period of 30 min. After stirring at 0 °C for 2 h, TLC analysis indicated incomplete reaction, so additional BH_3·THF (1.4 mL, 1.4 mmol) was added and the mixture was stirred for another 7 h. Then trimethylamine *N*-oxide dihydrate (TMNO, 1.60 g, 14.4 mmol) and diglyme (20 mL) were added and the mixture was heated with stirring to 100 °C for 17 h. During this time, THF distilled off. Another portion of TMNO (1.0 g, 9 mmol) was added and the mixture was heated to 150 °C and stirred for 8 h. After cooling, saturated aqueous NH_4Cl was added. The aqueous phase was extracted five times with CH_2Cl_2 (80 mL in total) and dried ($MgSO_4$). After removal of the solvent under reduced pressure, a colourless oil remained (^{13}C NMR, *dr* > 90:10), which was purified by flash chromatography (12 cm × 2.5 cm, petroleum ether/ethyl acetate, 4:6) to afford the hydration product **14** as a colourless oil (355 mg, 73%). $[\alpha]_D^{20}$ = –59.8 (*c* = 1.46, $CHCl_3$). IR (Film): $\tilde{\nu}$ = 3445 (b, OH), 2985, 2935, 2890, 1455 (C=N), 1375, 1255, 1220, 1150, 1065, 980, 900, 885, 840 cm^{-1}. ^{1}H NMR (250.1 MHz, $CDCl_3$): δ = 1.22 (d, $J_{5,Me}$ = 6.5 Hz, 3 H, 5-CH_3), 1.43, 1.45 [2 s, 6 H, $C(CH_3)_2$], 3.05 (br. s, 1 H, OH), 4.09 (dq, $J_{5,Me}$ = 6.5, $J_{5,6}$ = 3.9 Hz, 1 H, 5-H), 4.15 (br. dd, $J_{5,6}$ = 3.9, $J_{6,6a}$ = 2.0 Hz, 1 H, 6-H), 4.22 (dd, $J_{1',2'A}$ = 5.9, $J_{2'A,2'B}$ = 8.6 Hz, 1 H, 2′-H_A), 4.28 (dd, $J_{1',2'B}$ = 6.3, $J_{2'A,2'B}$ = 8.6 Hz, 1 H, 2′-H_B), 4.94 (dd, $J_{3a,6a}$ = 6.9, $J_{6,6a}$ = 2.0 Hz, 1 H, 6a-H), 4.97 ("t", $J_{1',2'A}$ = $J_{1',2'B}$ = 6.1 Hz, 1 H, 1′-H), 5.50 (d, $J_{3a,6a}$ = 7.5 Hz, 1 H, 3a-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 18.0 (5-CH_3), 25.5, 26.3 [$C(CH_3)_2$], 67.1 (C-2′), 70.2 (C-1′), 82.0 (C-6), 82.6 (C-5), 86.6 (C-3a), 91.4 (C-6a), 110.5 [$C(CH_3)_2$], 158.7 (C-3) ppm. $C_{11}H_{17}NO_5$ (243.3): calcd. C 54.31, H 7.04, N 5.76; found C 54.10, H 7.11, N 5.54.

(2*S*,3*R*,4*R*,5*R*,1′*R*,2′*S*)-2-(1′-*tert*-Butoxycarbonylamino-2′,3′-*O*-isopropylidenedioxypropyl)-3,4-dihydroxy-5-methyltetrahydrofuran (17): This compound was prepared following the procedure described for the preparation of **16**; lithium aluminium hydride (220 mg, 5.8 mmol) in dry diethyl ether (5 mL), isoxazoline **14** (282 mg, 1.16 mmol) in dry THF (4 mL), reaction time 16 h; hydrolysis with water (0.15 mL), 20% NaOH solution (0.1 mL), and water (0.5 mL) with stirring overnight; $MgSO_4$ (ca. 2 g) and stirring

for 5 h. Work up as described above provided the amino diol (*dr* > 95:5), which was dissolved in dioxane/water (2:1, 3 mL). Reaction with di-*tert*-butyl dicarbonate (500 mg, 2.29 mmol) for 16 h. The mixture was extracted with dichloromethane (five times, 80 mL total). The organic layer was washed with saturated potassium hydrogen carbonate solution (10 mL) and dried ($MgSO_4$). After removal of the solvent under reduced pressure and flash chromatography (8 cm × 2.5 cm, petroleum ether/ethyl acetate, 4:6), the *N*-Boc-amino diol **17** was obtained as a colourless wax (281 mg, 70%). $[\alpha]_D^{20}$ = +29.1 (*c* = 1.06, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3435 (b, OH), 2980, 2930, 1690, 1500, 1370, 1305, 1250, 1170, 1065 cm^{-1}. ^1H NMR (250.1 MHz, CD_3OD): δ = 1.31 (d, $J_{5,Me}$ = 7.1 Hz, 3 H, 5-CH_3), 1.32, 1.39 [2 s, 6 H, $C(CH_3)_2$], 1.44 [s, 9 H, $C(CH_3)_3$], 3.63, 3.85, 4.03 (3 m_c, 7 H, 1′-H, 2′-H, 3′-H_A, 3′-H_B, 2-H, 3-H, 4-H), 4.12 (q, $J_{5,Me}$ = 7.1 Hz, 1 H, 5-H) ppm. ^{13}C NMR (62.9 MHz, CD_3OD): δ = 19.1 (5-CH_3), 25.8, 27.0 [C(CH_3)$_2$], 28.8 [C(CH_3)$_3$], 54.8 (C-1′), 67.9 (C-3′), 77.1, 79.6, 80.5, 80.7, 84.1 (C-2, C-3, C-4, C-5, C-2′), 80.0 [$C(CH_3)_3$], 110.7 [$C(CH_3)_2$], 158.3 (C=O) ppm. $C_{16}H_{29}NO_7$ (347.4): calcd. C 55.32, H 8.41, N 4.03; found C 55.36, H 8.47, N 4.04.

(2*S*,3*R*,4*R*,5*R*,1′*R*,2′*S*)-2-(1′-*tert*-Butoxycarbonylamino-2′,3′-*O*-isopropylidenedioxypropyl)-5-methyl-3,4-bis(methylsulfonyloxy)tetrahydrofuran (20): This compound was prepared following the procedure described for the preparation of **19**; *N*-Boc-amino alcohol **17** (212 mg, 0.61 mmol), pyridine (3 mL), mesyl chloride (120 mL, 1.53 mmol); reaction time 16 h. Work up as described above and flash chromatography (12 cm × 2 cm, petroleum ether/ethyl acetate, 1:1) afforded **20** (298 mg, 97%) as an analytically pure, colourless foam, which was recrystallized from petroleum ether/ethyl acetate, 4:1, m.p. 144–146 °C. A crystal structure analysis was performed on this material.[32] $[\alpha]_D^{20}$ = –7.9 (*c* = 1.38, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3420 (b), 2980, 1709, 1511, 1368, 1336, 1180, 963, 858 cm^{-1}. ^1H NMR (500.1 MHz, C_6D_6): δ = 1.47 (d, $J_{5,Me}$ = 6.3 Hz, 3 H, 5-CH_3), 1.60 [s, 3 H, $C(CH_3)$], 1.71 [s, 9 H, $C(CH_3)_3$], 1.78 [s, 3 H, $C(CH_3)$], 2.84, 2.93 (2 s, 6 H, 2 H_3CSO_3), 3.96 (quint., $J_{4,5}$ = $J_{5,Me}$ = 6.3 Hz, 1 H, 5-H), 4.18, 4.38 (2 m_c, 4 H, 1′-H, 2′-H, 3′-H_A, 3′-H_B), 4.70 (dd, $J_{2,3}$ = 6.1, $J_{2,1'}$ = 1.2 Hz, 1 H, 2-H), 5.08 (dd, $J_{3,4}$ = 3.7, $J_{4,5}$ = 6.3 Hz, 1 H, 4-H), 5.13 (br. d, $J_{1',NH}$ = 9.8 Hz, 1 H, NH), 5.18 (dd, $J_{2,3}$ = 6.1, $J_{3,4}$ = 3.7 Hz, 1 H, 3-H) ppm. ^{13}C NMR (125.8 MHz, C_6D_6): δ = 17.7 (5-CH_3), 25.9, 27.4 [C(CH_3)$_2$], 28.7 [C(CH_3)$_3$], 37.7, 38.5 (H_3CSO_3), 51.8 (C-1′), 67.8 (C-3′), 76.4 (C-2′), 76.8 (C-2), 78.0 (C-5), 80.1 [$C(CH_3)_3$], 82.6 (C-3), 87.6 (C-4), 110.5 [$C(CH_3)_2$], 155.9 (s, C=O) ppm. $C_{18}H_{33}NO_{11}S_2$ (503.6): calcd. C 42.93, H 6.61, N 2.78, S 12.73; found C 42.80, H 6.66, N 2.56, S 12.82.

(2*R*,5*R*,1′*S*,2′*S*)-2-(1′-*tert*-Butoxycarbonylamino-2′,3′-*O*-isopropylidenedioxypropyl)-5-methyl-2,5-dihydrofuran (23): According to the procedure described in ref.[35], sodium (280 mg, 12.2 mmol) and naphthalene (1.56 g, 12 mmol) were dissolved in dry THF (12 mL) under nitrogen and stirred for 3 h at room temp. The dimesylate **20** (233 mg, 0.46 mmol) was dissolved in dry THF (3 mL) under nitrogen at 0 °C, to which the sodium/naphthalene reagent (2 mL) was added very quickly (1–2 s) by syringe in order to maintain the green colour of the reagent. After stirring for 30 min, the reaction was quenched with methanol (0.4 mL) and water (1 mL). Stirring was continued for 10 min and then a saturated aqueous solution of NH_4Cl (20 mL) was added. The reaction mixture was extracted with CH_2Cl_2 (five times, 80 mL total) and dried ($MgSO_4$). After evaporation of the solvent, the residue was purified by flash chromatography (10 cm × 2.5 cm, petroleum ether/ethyl acetate, 4:1) to afford a colourless oil, which was crystallized from *n*-heptane to provide **23** as a colourless solid (125 mg, 75%), m.p. 80–81 °C. $[\alpha]_D^{20}$ = +106 (*c* = 1.29, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2983, 2864, 1711, 1505, 1369, 1288, 1251, 1209, 1174, 1076, 1047, 861, 846 cm^{-1}. ^1H NMR (300.1 MHz, $CDCl_3$): δ = 1.30 (d, $J_{5,Me}$ = 6.4 Hz, 3 H, 5-CH_3), 1.36 [s, 3 H, $C(CH_3)$], 1.41 [s, 9 H, $C(CH_3)_3$], 1.43 [s, 3 H, $C(CH_3)$], 3.74 (m, 1 H, 1′-H), 3.90, 4.08 (2 m_c, 3 H, 2′-H, 3′-H_A, 3′-H_B), 4.57 (br. d, $J_{1',NH}$ = 10.2 Hz, 1 H, NH), 4.94 (dddq, $J_{2,5}$ = 4.5, $J_{3,5}$ = 2.4, $J_{4,5}$ = 1.3, $J_{5,Me}$ = 6.4 Hz, 1 H, 5-H), 5.13 (dddd, $J_{2,3}$ = 1.5, $J_{2,4}$ = 2.5, $J_{2,5}$ = 4.5, $J_{2,1'}$ = 1.3 Hz, 1 H, 2-H), 5.70 (ddd, $J_{2,3}$ = 1.6, $J_{3,4}$ = 6.1, $J_{3,5}$ = 2.3 Hz, 1 H, 3-H), 5.80 (ddd, $J_{2,4}$ = 2.5, $J_{3,4}$ = 6.1, $J_{4,5}$ = 1.4 Hz, 1 H, 4-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 22.0 (5-CH_3), 25.5, 26.8 [C(CH_3)$_2$], 28.3 [C(CH_3)$_3$], 54.7 (C-1′), 67.8 (C-3′), 75.4 (C-2′), 79.4 [$C(CH_3)_3$], 82.1 (C-5), 85.1 (C-2), 109.7 [$C(CH_3)_2$], 127.4 (C-3), 132.7 (C-4), 156.0 (C=O) ppm. $C_{16}H_{27}NO_5$ (313.4): calcd. C 61.32, H 8.68, N 4.47; found C 61.53, H 8.70, N 4.32.

(2*R*,5*R*,1′*S*,2′*S*)-2-(1′-*tert*-Butoxycarbonylamino-2′,3′-dihydroxypropyl)-5-methyl-2,5-dihydrofuran (26): This compound was prepared following the procedure described for the preparation of **25**; olefin **23** (424 mg, 1.35 mmol) in methanol (4 mL)/water (1 mL)/trifluoroacetic acid (0.1 mL); reaction time 30 h. Work up as described above for **25** and elution through a pad of silica (6 cm × 2.5 cm, petroleum ether/ethyl acetate, 1:1) afforded **26** as a colourless solid (344 mg, 93%), m.p. 75–76 °C. $[\alpha]_D^{20}$ = +103 (*c* = 1.32, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3443, 3407, 2976, 1699, 1675, 1516, 1369, 1346, 1287, 1247, 1174, 1083, 1058, 999, 762 cm^{-1}. ^1H NMR (500.1 MHz, CD_3OD, 333 K): δ = 1.30 (d, $J_{5,Me}$ = 6.4 Hz, 3 H, 5-CH_3), 1.42 [s, $C(CH_3)_3$], 3.52, 3.61, 3.68 (3 m_c, 4 H, 1′-H, 2′-H, 3′-H_A, 3′-H_B), 4.89 (dddq, $J_{2,5}$ = 4.2, $J_{3,5}$ = 2.3, $J_{4,5}$ = 1.4, $J_{5,Me}$ = 6.4 Hz, 1 H, 5-H), 5.18 (dd“t”, $J_{2,3}$ = $J_{2,1'}$ = 1.5, $J_{2,4}$ = 2.4, $J_{2,5}$ = 4.2 Hz, 1 H, 2-H), 5.71 (ddd, $J_{2,3}$ = 1.4, $J_{3,4}$ = 6.1, $J_{3,5}$ = 2.3 Hz, 1 H, 3-H), 5.83 (ddd, $J_{2,4}$ = 2.4, $J_{3,4}$ = 6.1, $J_{4,5}$ = 1.4 Hz, 1 H, 4-H) ppm. ^{13}C NMR (125.8 MHz, CD_3OD, 333 K): δ = 22.8 (5-CH_3), 29.4 [C(CH_3)$_3$], 55.9 (C-1′), 65.8 (C-3′), 73.7 (C-2′), 81.1 [$C(CH_3)_3$], 84.1 (C-5), 86.9 (C-2), 129.5 (C-3), 134.0 (C-4), 158.8 (C=O) ppm. $C_{13}H_{23}NO_5$ (273.3): calcd. C 57.13, H 8.48, N 5.12; found C 57.08, H 8.46, N 5.07.

(2*S*,2′*R*,5′*R*)-2-(*tert*-Butoxycarbonylamino)-2-(5′-methyl-2′,5′-dihydrofuran-2-yl)acetic Acid (29): This compound was prepared following the procedure described for the preparation of **28**; diol **26** (278 mg, 1.02 mmol) in methanol (3 mL)/water (3 mL), sodium periodate (261 mg, 1.22 mmol); reaction time 15 min. Work up as described above for **28**. The resulting aldehyde was dissolved in *tert*-butyl alcohol (5 mL)/2-methyl-2-butene (3 mL) and treated with sodium chlorite ($NaClO_2$, 184 mg, 1.53 mmol) and sodium dihydrogen phosphate (184 mg, 1.53 mmol) in water (1.5 mL); addition time 45 min, reaction time 2 h at room temp. Work up as described above provided the *N*-Boc-amino acid **29** as a colourless solid (245 mg, 93%), m.p. 95–100 °C. $[\alpha]_D^{20}$ = +91.5 (*c* = 1.47, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3441, 3083, 2981, 1747, 1733, 1673, 1520, 1406, 1370, 1356, 1251, 1207, 1166, 1092, 1071, 858 cm^{-1}. ^1H NMR (300.1 MHz, $CDCl_3$, 323 K): δ = 1.31 (d, $J_{5',Me}$ = 6.4 Hz, 3 H, 5′-CH_3), 1.43 [s, $C(CH_3)_3$], 4.49 (br. d, $J_{2,NH}$ = 9.1 Hz, 1 H, 2-H), 4.93 (dddq, $J_{2',5'}$ = 4.1, $J_{3',5'}$ = 2.3, $J_{4',5'}$ = 1.4, $J_{5',Me}$ = 6.4 Hz, 1 H, 5′-H), 5.12 (br. d, $J_{2,NH}$ = 9.1 Hz, 1 H, NH), 5.31 (dd“t”, $J_{2,2'}$ = $J_{2',4'}$ = 2.4, $J_{2',3'}$ = 1.4, $J_{2',5'}$ = 4.1 Hz, 1 H, 2′-H), 5.76 (ddd, $J_{2',3'}$ = 1.4, $J_{3',4'}$ = 6.2, $J_{3',5'}$ = 2.3 Hz, 1 H, 3′-H), 5.86 (ddd, $J_{2',4'}$ = 2.3, $J_{3',4'}$ = 6.2, $J_{4',5'}$ = 1.4 Hz, 1 H, 4′-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$, 323 K): δ = 21.8 (5′-CH_3), 28.4 [C(CH_3)$_3$], 56.1 (C-2), 80.2 [$C(CH_3)_3$], 82.8 (C-5′), 86.7 (C-2′), 126.3 (C-3′), 133.6 (C-4′), 155.7 (C=O), 173.7 (C-1) ppm. $C_{12}H_{19}NO_5$ (257.3): calcd. C 56.02, H 7.44, N 5.44; found C 56.00, H 7.45, N 5.22.

(2*S*,2′*R*,5′*R*)-2-Amino-2-(5′-methyl-2′,5′-dihydrofuran-2′-yl)acetic Acid, (–)-5′-*epi*-Furanomycin (2): This compound was prepared fol-

lowing the procedure described for the preparation of **1**; *N*-Boc-amino acid **29** (222 mg, 0.86 mmol), HCl in dioxane (6 N, 3 mL), reaction time 2.5 h at room temp. Work up as described above provided an orange-coloured solid, which was recrystallized from ethanol. Compound **2** (81 mg, 60%) was obtained as a colourless solid, m.p. 174–177 °C; lit.[13]: 175–178 °C. $[\alpha]_D^{20}$ = –53 (*c* = 0.10, H_2O); lit.[13]: $[\alpha]_D^{20}$ = –50 (*c* = 0.1, H_2O). IR (KBr): $\tilde{\nu}$ = 3480 (b), 3137, 2963, 2876, 1632, 1568, 1523, 1401, 1384, 1349, 1088, 1054, 1019, 730 cm^{-1}. ^1H NMR (500.1 MHz, D_2O): δ = 1.18 (d, $J_{5',Me}$ = 6.5 Hz, 3 H, 5′-CH_3), 3.74 (d, $J_{2,2'}$ = 3.2 Hz, 1 H, 2-H), 4.86 (dddq, $J_{2',5'}$ = 4.4, $J_{3',5'}$ = 2.4, $J_{4',5'}$ = 1.4, $J_{5',Me}$ = 6.5 Hz, 1 H, 5′-H), 5.17 (dddd, $J_{2,2'}$ = 3.2, $J_{2',3'}$ = 1.5, $J_{2',4'}$ = 2.5, $J_{2',5'}$ = 4.4 Hz, 1 H, 2′-H), 5.73 (ddd, $J_{2',3'}$ = 1.5, $J_{3',4'}$ = 6.2, $J_{3',5'}$ = 2.4 Hz, 1 H, 3′-H), 6.01 (ddd, $J_{2',4'}$ = 2.5, $J_{3',4'}$ = 6.2, $J_{4',5'}$ = 1.4 Hz, 1 H, 4′-H) ppm. ^{13}C NMR (125.8 MHz, D_2O): δ = 21.1 (5′-CH_3), 57.3 (C-2), 83.6, 84.5 (C-2′, C-5′), 124.9 (C-3′), 135.9 (C-4′), 172.0 (C-1) ppm. $C_7H_{11}NO_3$ (157.2): calcd. C 53.50, H 7.05, N 8.91; found C 53.16, H 7.06, N 8.57. MS (FAB pos., glycerol, 345 K): *m*/*z* (%) = 158 (100) $[M + H]^+$, 315 (20) $[2M + H]^+$. HRMS (FAB pos.): $C_7H_{12}NO_3$, $[M + H]^+$: calcd. 158.0817, found 158.0821.

(3a*S*,6*R*,6a*R*,1′*S*)-6-Hydroxy-3-(1′,2′-*O*-isopropylidenedioxyethyl)-5,5-dimethyl-3a,5,6,6a-tetrahydrofuro[2,3-*d*]isoxazole (15): A solution of methylmagnesium bromide (3 M, 0.5 mL) was diluted in THF (5 mL) under nitrogen and cooled to –40 °C. A solution of epoxide **11** (241 mg, 1.00 mmol) in CH_2Cl_2 (5 mL) was then added dropwise to this solution. After stirring for 15 min, the reaction was quenched with saturated aqueous NH_4Cl solution, extracted with CH_2Cl_2 (3 × 20 mL), and dried over $MgSO_4$. After concentration of the solvent in vacuo the residue was purified by flash chromatography (10 cm × 2.5 cm, petroleum ether/ethyl acetate, 7:3) to afford the isoxazoline **15** as a colourless oil (214 mg, 83%). $[\alpha]_D^{20}$ = –60.9 (*c* = 1.50, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3450 (b), 2985, 2937, 1461, 1373, 1250, 1217, 1152, 1064, 983, 899, 844, 802 cm^{-1}. ^1H NMR (500.1 MHz, $CDCl_3$): δ = 1.22, 1.27 (2 s, 6 H, 5-CH_3), 1.42, 1.43 [2 s, 6 H, $C(CH_3)_2$], 2.17 (br. s, 1 H, OH), 4.08 (d, $J_{6,6a}$ = 2.1 Hz, 1 H, 6-H), 4.27 (m_c, 2 H, 2′-H_A, 2′-H_B), 4.94 (dd, $J_{3a,6a}$ = 7.8, $J_{6,6a}$ = 2.1 Hz, 1 H, 6a-H), 4.94 ("t", $J_{1',2'A}$ = $J_{1',2'B}$ = 6.0 Hz, 1 H, 1′-H), 5.50 (d, $J_{3a,6a}$ = 7.8 Hz, 1 H, 3a-H) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 21.9, 25.3, 25.5, 26.2 [2 5-CH_3, $C(CH_3)_2$], 67.0 (C-2′), 70.1 (C-1′), 82.6 (C-6), 85.2 (C-3a), 85.3 (C-5), 91.4 (C-6a), 110.4 [$C(CH_3)_2$], 158.8 (C-3) ppm. $C_{12}H_{19}NO_5$ (257.3): calcd. C 56.02, H 7.45, N 5.44; found C 56.10, H 7.56, N 5.32.

(2*S*,3*R*,4*S*,1′*R*,2′*S*)-2-(1′-*tert*-Butoxycarbonylamino-2′,3′-*O*-isopropylidenedioxypropyl)-3,4-dihydroxy-5,5-dimethyltetrahydrofuran (18): This compound was prepared following the procedure described for the preparation of **16**; lithium aluminium hydride (283 mg, 7.5 mmol) in THF (5 mL), isoxazoline **15** (480 mg, 1.87 mmol) in diethyl ether (5 mL), reaction time 16 h; hydrolysis with water (0.2 mL), 20% NaOH solution (0.2 mL), and water (0.7 mL) with stirring for 1.5 h; $MgSO_4$ (ca. 3 g), stirring for 4 h. Work up as described above provided the amino diol (*dr* > 95:5), which was dissolved in dioxane/water (2:1, 6 mL). Reaction with di-*tert*-butyl dicarbonate (610 mg, 2.8 mmol) for 16 h. Citric acid solution (1 N, 15 mL) was added and the mixture was extracted with dichloromethane (five times, 125 mL total). The organic layer was washed with saturated potassium hydrogen carbonate solution (10 mL) and dried ($MgSO_4$). After removal of the solvent under reduced pressure and flash chromatography (14 cm × 2.5 cm, petroleum ether/ethyl acetate, 1:1), the *N*-Boc-amino diol **18** (435 mg, 65%) was obtained as a colourless solid, m.p. 151–152 °C. $[\alpha]_D^{20}$ = +18.5 (*c* = 1.52, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3459, 3385, 2977, 2929, 2915, 1703, 1509, 1372, 1304, 1269, 1241, 1230, 1164, 1126, 1067, 917, 850 cm^{-1}. ^1H NMR (500.1 MHz, CD_3OD, 333 K): δ = 1.14, 1.30, 1.32, 1.39 [4 s, 12 H, $C(CH_3)_2$, 2 5-CH_3], 1.45 [s, 9 H, $C(CH_3)_3$], 3.63 (d, $J_{3,4}$ = 5.6 Hz, 1 H, 4-H), 3.85 (m_c, 2 H, 1′-H, 3′-H_A), 4.02 (dd, $J_{2',3'B}$ = 6.3, $J_{3'A,3'B}$ = 8.4 Hz, 1 H, 3′-H_B), 4.09 (ddd, $J_{1',2'}$ = 2.8, $J_{2',3'A}$ = 5.7, $J_{2',3'B}$ = 6.3 Hz, 1 H, 2′-H), 4.16 (dd, $J_{2,3}$ = 6.8, $J_{3,4}$ = 5.6 Hz, 1 H, 3-H), 4.21 (dd, $J_{2,3}$ = 6.8, $J_{1',2}$ = 2.6 Hz, 1 H, 2-H) ppm. ^{13}C NMR (125.8 MHz, CD_3OD, 333 K): δ = 22.1, 25.8, 27.1, 27.5 [$C(CH_3)_2$, 5-CH_3], 28.9 [$C(CH_3)_3$], 53.4 (C-1′), 68.3 (C-3′), 77.1 (C-2′), 77.4 (C-2), 79.3 (C-3), 80.7 [$C(CH_3)_3$], 81.7 (C-5), 84.6 (C-4), 110.8 [$C(CH_3)_2$], 158.2 (C=O) ppm. $C_{17}H_{31}NO_7$ (361.4): calcd. C 56.49, H 8.64, N 3.88; found C 56.49, H 8.74, N 3.87.

(2*S*,3*R*,4*S*,1′*R*,2′*S*)-2-(1′-*tert*-Butoxycarbonylamino-2′,3′-*O*-isopropylidenedioxypropyl)-5,5-dimethyl-3,4-bis(methylsulfonyloxy)tetrahydrofuran (21): This compound was prepared following the procedure described for the preparation of **19**; *N*-Boc-amino alcohol **18** (346 mg, 0.96 mmol), pyridine (5 mL), mesyl chloride (190 µL, 2.40 mmol), reaction time 16 h. Work up as described above for **19** and flash chromatography (14 cm × 2.5 cm, petroleum ether/ethyl acetate, 6:4) afforded **21** (458 mg, 92%) as an analytically pure, colourless foam, which was recrystallized from heptane/ethyl acetate (4:1), m.p. 140–141 °C. A crystal structure analysis was performed on this material.[33] $[\alpha]_D^{20}$ = –35.1 (*c* = 1.27, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2974, 1704, 1513, 1371, 1360, 1338, 1265, 1241, 1221, 1177, 1065, 1049, 1027, 1013, 981, 961, 875, 849 cm^{-1}. ^1H NMR (500.1 MHz, C_6D_6, 343 K): δ = 1.39, 1.60, 1.62 [3 s, 9 H, 2 5-CH_3, $C(CH_3)$], 1.74 [s, 9 H, $C(CH_3)_3$], 1.79 [s, 3 H, $C(CH_3)$], 2.93, 3.07 (2 s, 6 H, 2 H_3CSO_3), 4.23, 4.38 (2 m_c, 4 H, 1′-H, 2′-H, 3′-H_A, 3′-H_B), 4.94 (dd, $J_{2,3}$ = 7.1, $J_{2,1'}$ = 1.1 Hz, 1 H, 2-H), 5.11 (br. d, $J_{1',NH}$ = 9.8 Hz, 1 H, NH), 5.26 (d, $J_{3,4}$ = 5.5 Hz, 1 H, 4-H), 5.54 (dd, $J_{2,3}$ = 7.1, $J_{3,4}$ = 5.5 Hz, 1 H, 3-H) ppm. ^{13}C NMR (125.8 MHz, C_6D_6): δ = 21.6, 25.7, 26.2, 27.2 [2 5-CH_3, $C(CH_3)_2$], 28.5 [$C(CH_3)_3$], 37.8, 38.5 (2 H_3CSO_3), 51.9 (C-1′), 67.4 (C-3′), 73.8 (C-2), 75.7 (C-2′), 79.8 [$C(CH_3)_3$], 80.0 (C-5), 81.0 (C-3), 87.4 (C-4), 110.3 [$C(CH_3)_2$], 155.5 (C=O) ppm. $C_{19}H_{35}NO_{11}S_2$ (517.6): calcd. C 44.09, H 6.82, N 2.71, S 12.39; found C 44.01, H 6.75, N 2.68, S 12.54.

(2*R*,1′*S*,2′*S*)-2-(1′-*tert*-Butoxycarbonylamino-2′,3′-*O*-isopropylidenedioxypropyl)-5,5-dimethyl-2,5-dihydrofuran (24): This compound was prepared following the procedure described for the preparation of **22**; sodium (280 mg, 12.2 mmol) and naphthalene (1.56 g, 12 mmol) were dissolved in dry THF (12 mL) under nitrogen and stirred for 3 h at room temp. A portion (8 mL) of this solution was then transferred to another round-bottomed flask by syringe, and a solution of the dimesylate **21** (520 mg, 1.0 mmol) in dry THF (7 mL) was added dropwise under nitrogen at 0 °C. After stirring for 15 min, the reaction was quenched with methanol (0.3 mL) and saturated NH_4Cl solution (20 mL) was added. Work up as described above for **22** and flash chromatography (15 cm × 2.5 cm, petroleum ether/ethyl acetate, 4:1) afforded a colourless solid **24** (267 mg, 81%), m.p. 104–107 °C. $[\alpha]_D^{20}$ = +155 (*c* = 1.30, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3361, 2979, 1687, 1525, 1456, 1395, 1371, 1352, 1340, 1314, 1297, 1249, 1221, 1163, 1108, 1079, 1057, 1038, 1024, 1006, 957, 909, 871, 853, 829, 794, 732 cm^{-1}. ^1H NMR (300.1 MHz, $CDCl_3$): δ = 1.30, 1.36 [2 s, 9 H, 2 5-CH_3, $C(CH_3)$], 1.41 [s, 9 H, $C(CH_3)_3$], 1.42 [s, 3 H, $C(CH_3)$], 3.71 (br. m, 1 H, 1′-H), 3.90, 4.06 (2 m_c, 3 H, 2′-H, 3′-H_A, 3′-H_B), 4.62 (br. d, $J_{1',NH}$ = 10.2 Hz, 1 H, NH), 5.15 (d"t", $J_{2,3}$ = $J_{2,1'}$ = 1.3, $J_{2,4}$ = 2.4 Hz, 1 H, 2-H), 5.60 (dd, $J_{2,3}$ = 1.4, $J_{3,4}$ = 6.0 Hz, 1 H, 3-H), 5.79 (dd, $J_{2,4}$ = 2.4, $J_{3,4}$ = 6.0 Hz, 1 H, 4-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 25.6, 26.9, 28.0, 28.2 [2 5-CH_3, $C(CH_3)_2$], 28.3 [$C(CH_3)_3$], 54.9 (C-1′), 67.7 (C-3′), 75.5 (C-2′), 79.4 [$C(CH_3)_3$], 84.0 (C-2), 88.0 (C-5), 109.7 [$C(CH_3)_2$], 125.9 (C-3), 136.7 (C-4), 156.1

(C=O) ppm. $C_{17}H_{29}NO_5$ (327.4): calcd. C 62.36, H 8.93, N 4.28; found C 62.60, H 8.63, N 4.40.

(2*R*,1′*S*,2′*S*)-2-(1′-*tert*-Butoxycarbonylamino-2′,3′-dihydroxypropyl)-5,5-dimethyl-2,5-dihydrofuran (27): This compound was prepared following the procedure described for the preparation of **25**; olefin **24** (327 mg, 1.0 mmol) in methanol (4 mL)/water (1 mL)/trifluoroacetic acid (0.15 mL); reaction time 20 h. Work up as described above and elution through a pad of silica (11 cm × 2.5 cm, petroleum ether/ethyl acetate, 4:6) afforded diol **27** as a colourless solid (247 mg, 86%), m.p. 146–149 °C. $[\alpha]_D^{20}$ = +163 (*c* = 1.41, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3514, 3371, 2985, 2971, 1694, 1521, 1436, 1393, 1364, 1348, 1306, 1253, 1232, 1188, 1165, 1093, 1070, 1054, 1039, 1024, 1010, 879, 872, 828 cm^{-1}. ^1H NMR (500.1 MHz, CD_3OD, 333 K): δ = 1.28, 1.37 (2 s, 6 H, 2 5-CH_3), 1.42 [s, $C(CH_3)_3$], 3.55, 3.63, 3.69 (3 m_c, 4 H, 1′-H, 2′-H, 3′-H_A, 3′-H_B), 5.21 (d"t", $J_{2,3}$ = $J_{2,1'}$ = 1.5, $J_{2,4}$ = 2.5 Hz, 1 H, 2-H), 5.62 (dd, $J_{2,3}$ = 1.4, $J_{3,4}$ = 6.1 Hz, 1 H, 3-H), 5.82 (dd, $J_{2,4}$ = 2.5, $J_{3,4}$ = 6.1 Hz, 1 H, 4-H) ppm. ^{13}C NMR (125.8 MHz, CD_3OD, 333 K): δ = 28.3, 28.6 (2 5-CH_3), 28.7 [C(CH_3)$_3$], 55.2 (C-1′), 65.1 (C-3′), 72.7 (C-2′), 80.3 [$C(CH_3)_3$], 85.2 (C-2), 89.3 (C-5), 127.4 (C-3), 137.4 (C-4), 158.3 (C=O) ppm. $C_{14}H_{25}NO_5$ (287.3): calcd. C 58.52, H 8.77, N 4.87; found C 58.49, H 8.72, N 4.88.

(2*S*,2′*R*)-2-(*tert*-Butoxycarbonylamino)-2-(5′,5′-dimethyl-2′,5′-dihydrofuran-2′-yl)acetic Acid (30): This compound was prepared following the procedure described for the preparation of **28**; diol **27** (239 mg, 0.83 mmol) in methanol (3 mL)/water (3 mL), sodium periodate (214 mg, 1.00 mmol); reaction time 20 min and work up as described above. The aldehyde was treated with *tert*-butyl alcohol (5 mL)/2-methyl-2-butene (3 mL), sodium chlorite ($NaClO_2$, 183 mg, 2.00 mmol), and sodium dihydrogen phosphate (200 mg, 2.00 mmol) in water (2 mL); addition time 50 min, reaction time 2 h at room temp. Work up as described above provided the *N*-Boc-amino acid **30** as a colourless solid (209 mg, 93%), m.p. 140–141 °C. $[\alpha]_D^{20}$ = +152 (*c* = 1.20, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3396, 3127, 3068, 2996, 2971, 2933, 1749, 1707, 1499, 1405, 1363, 1346, 1165, 1057 cm^{-1}. ^1H NMR (300.1 MHz, $CDCl_3$, 323 K): δ = 1.30, 1.38 (2 s, 6 H, 2 5′-CH_3), 1.43 [s, $C(CH_3)_3$], 4.47 (br. dd, $J_{2,2'}$ = 2.4, $J_{2,NH}$ = 9.1 Hz, 1 H, 2-H), 5.15 (br. d, $J_{2,NH}$ = 9.1 Hz, 1 H, NH), 5.34 (d"t", $J_{2,2'}$ = $J_{2',4'}$ = 2.4, $J_{2',3'}$ = 1.4 Hz, 1 H, 2′-H), 5.66 (dd, $J_{2',3'}$ = 1.4, $J_{3',4'}$ = 6.0 Hz, 1 H, 3′-H), 5.83 (dd, $J_{2',4'}$ = 2.4, $J_{3',4'}$ = 6.0 Hz, 1 H, 4′-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$, 323 K): δ = 27.7, 28.1 (2 5′-CH_3), 28.4 [C(CH_3)$_3$], 56.2 (C-2), 80.1 [$C(CH_3)_3$], 85.8 (C-2′), 89.2 (C-5′), 124.8 (C-3′), 137.6 (C-4′), 155.7 (C=O), 173.6 (C-1) ppm. $C_{13}H_{21}NO_5$ (271.3): calcd. C 57.55, H 7.80, N 5.16; found C 57.61, H 7.79, N 5.03.

(2*S*,2′*R*)-2-Amino-2-(5′,5′-dimethyl-2′,5′-dihydrofuran-2′-yl)acetic Acid (3): This compound was prepared following the procedure described for the preparation of **1**; *N*-Boc-amino acid **30** (160 mg, 0.59 mmol), HCl (6 N, 1.5 mL) in methanol/water (3:2, 5 mL); reaction time 3 h at room temp. Work up as described above gave a colourless solid, which was recrystallized from water/acetone to yield a colourless solid **3** (57 mg, 56%), m.p. 179–183 °C. $[\alpha]_D^{20}$ = +73 (*c* = 0.25, H_2O). IR (KBr): $\tilde{\nu}$ = 3450, 3028, 2967, 2929, 2609, 1622, 1538, 1461, 1437, 1404, 1360, 1345, 1109, 1096, 1042, 1025, 829, 775 cm^{-1}. ^1H NMR (500.1 MHz, D_2O): δ = 1.22, 1.28 (2 s, 6 H, 2 5′-CH_3), 3.75 (d, $J_{2,2'}$ = 3.1 Hz, 1 H, 2-H), 5.25 (ddd, $J_{2,2'}$ = 3.1, $J_{2',3'}$ = 1.5, $J_{2',4'}$ = 2.4 Hz, 1 H, 2′-H), 5.67 (dd, $J_{2',3'}$ = 1.5, $J_{3',4'}$ = 6.1 Hz, 1 H, 3′-H), 6.04 (dd, $J_{2',4'}$ = 2.4, $J_{3',4'}$ = 6.1 Hz, 1 H, 4′-H) ppm. ^{13}C NMR (125.8 MHz, D_2O): δ = 26.7, 27.3 (2 5′-CH_3), 57.2 (C-2), 83.5 (C-2′), 90.4 (C-5′), 123.4 (C-3′), 139.9 (C-4′), 172.0 (C-1) ppm. $C_8H_{13}NO_3$ (171.2): calcd. C 56.13, H 7.65, N 8.18; found C 55.73, H 7.73, N 8.05. MS (FAB pos., glycerol, 335 K): *m*/*z* (%) = 172 (100) $[M + H]^+$, 343 (25) $[2M + H]^+$. HRMS (FAB pos.): $C_7H_{12}NO_3$, $[M + H]^+$: calcd. 172.0974, found 172.0972.

(2*R*,5*S*,1′*S*,2′*S*)-2-(1′-*tert*-Butoxycarbonylamino-2′,3′-*O*-isopropylidenedioxypropyl)-5-methyltetrahydrofuran (31): Dihydrofuran **22** (100 mg, 0.32 mmol) was dissolved in dry methanol (20 mL) in a Parr bottle and 10% Pd/C (50 mg) was added under nitrogen. After hydrogenolysis for 4 h at 1 bar, the catalyst was filtered off and the solvent was removed in vacuo. The residue was purified by flash chromatography (16 cm × 2.5 cm, petroleum ether/ethyl acetate, 4:1) to afford the *N*-Boc-tetrahydrofuran derivative **31** as a colourless solid (80 mg, 80%), m.p. 73–74 °C. $[\alpha]_D^{20}$ = +25.2 (*c* = 1.32, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3340, 2960, 1670, 1505, 1350, 1225, 1150, 1050 cm^{-1}. ^1H NMR (300.1 MHz, $CDCl_3$, 323 K): δ = 1.19 (d, $J_{5,Me}$ = 6.1 Hz, 3 H, 5-CH_3), 1.35, 1.40 [2 s, 6 H, $C(CH_3)_2$], 1.44 [s, 9 H, $C(CH_3)_3$], 1.51, 1.70, 1.98 (3 m, 4 H, 3-H_A, 3-H_B, 4-H_A, 4-H_B), 3.65 (m, 1 H, 1′-H), 3.87 (dd, $J_{2',3'A}$ = 5.9, $J_{3'A,3'B}$ = 8.2 Hz, 1 H, 3′-H_A), 4.01 (dd, $J_{2',3'B}$ = 6.1, $J_{3'A,3'B}$ = 8.2 Hz, 1 H, 3′-H_B), 4.05 (m, 1 H, 2′-H), 4.10 (ddq, $J_{5,Me}$ = 6.2, $J_{4A,5}$ = 6.2, $J_{4B,5}$ = 8.1 Hz, 1 H, 5-H), 4.29 (ddd, $J_{2,1'}$ = 1.4, $J_{2,3A}$ = 6.2, $J_{2,3B}$ = 8.1 Hz, 1 H, 2-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$, 323 K): δ = 21.4 (q, 5-CH_3), 25.7, 26.8 [2 q, C(CH_3)$_2$], 28.4 [q, C(CH_3)$_3$], 29.1, 34.0 (2 d, C-3, C-4), 55.5 (d, C-1′), 67.4 (t, C-3′), 76.5, 76.5, 76.8 (3 d, C-2, C-2′, C-5), 79.5 [s, $C(CH_3)_3$], 110.0 [s, $C(CH_3)_2$], 156.3 (s, C=O) ppm. $C_{16}H_{29}NO_5$ (313.4): calcd. C 60.93, H 9.27, N 4.44; found C 60.86, H 9.16, N 4.38.

(2*R*,5*S*,1′*S*,2′*S*)-2-(1′-*tert*-Butoxycarbonylamino-2′,3′-dihydroxypropyl)-5-methyltetrahydrofuran (32): Trifluoroacetic acid (0.15 mL) was added to a solution of the acetonide **31** (204 mg, 0.647 mmol) in methanol (4 mL) and water (1 mL). After stirring for 27 h the mixture was neutralized with aqueous ammonia (1 N, 5 mL), then silica gel (0.2 g) was added and the solvent was evaporated. The silica gel with the adsorbed product was loaded onto the top of a column of silica gel and purified by chromatography (14 cm × 2.5 cm, petroleum ether/ethyl acetate, 4:6) to afford the diol **32** as a colourless wax (137 mg, 77%). $[\alpha]_D^{20}$ = +16.3 (*c* = 0.445, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3450 (b), 2969, 2933, 1691, 1500, 1457, 1392, 1172, 1065 cm^{-1}. ^1H NMR (300.1 MHz, CD_3OD, 333 K): δ = 1.19 (d, $J_{5,Me}$ = 6.1 Hz, 3 H, 5-CH_3), 1.45 [s, $C(CH_3)_3$], 1.57, 1.74, 2.02 (3 m, 4 H, 3-H_A, 3-H_B, 4-H_A, 4-H_B), 3.48 (m, 1 H, 1′-H), 3.49 (d, $J_{3'A,3'B}$ = 11.4 Hz, 1 H, 3′-H_A), 3.60 (dd, $J_{2',3'A}$ = 5.8, $J_{2',3'B}$ = 3.2 Hz, 1 H, 2′-H), 3.64 (dd, $J_{2',3'B}$ = 3.2, $J_{3'A,3'B}$ = 11.2 Hz, 1 H, 3′-H_B), 4.12 (ddq, $J_{4A,5}$ = $J_{5,Me}$ = 6.0, $J_{4B,5}$ = 8.0, 1 H, 5-H), 4.44 (ddd, $J_{2,3A}$ = 6.5, $J_{2,3B}$ = 8.8, $J_{2,1'}$ = 1.8 Hz, 1 H, 2-H) ppm. ^{13}C NMR (75.5 MHz, CD_3OD, 333 K): δ = 21.5 (q, 5-CH_3), 28.7 [q, C(CH_3)$_3$], 29.9, 34.9 (2 t, 3-C, 4-C), 55.7 (d, C-1′), 65.0 (t, C-3′), 73.5, 77.5, 77.6 (3 d, C-2, C-5, C-2′), 80.3 [s, $C(CH_3)_3$], 158.8 (s, C=O) ppm. $C_{13}H_{25}NO_5$ (275.4): calcd. C 56.71, H 9.16, N 5.09; found C 56.48, H 9.25, N 5.09.

(2*S*,2′*R*,5′*S*)-2-(*tert*-Butoxycarbonylamino)-2-(5′-methyltetrahydrofuran-2′-yl)acetic Acid, *N*-Boc-Dihydrofuranomycin (33): This compound was prepared following the procedure described for the preparation of **28**; diol **32** (125 mg, 0.454 mmol) in isopropyl alcohol/water (3:1, 8 mL), sodium periodate (117 mg, 0.545 mmol); reaction time 15 min. Work up as described above for **28**. The resulting aldehyde was dissolved in *tert*-butyl alcohol (5 mL)/2-methyl-2-butene (2 mL) and treated with sodium chlorite ($NaClO_2$, 82 mg, 0.91 mmol) and sodium dihydrogen phosphate (125 mg, 0.91 mmol) in water (1.5 mL); addition time 3.5 h, reaction time 16 h at room temp. Work up as described above for **28** provided the *N*-Boc-amino acid **33** as a slightly yellow solid (88 mg, 75%), m.p. 133–134 °C. $[\alpha]_D^{20}$ = +18.9 (*c* = 1.14, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3449, 3090, 2982, 2928, 1751, 1738, 1670, 1524, 1258, 1165, 1183,

860 cm^{-1}. ^1H NMR (300.1 MHz, $CDCl_3$, 323 K): δ = 1.22 (d, $J_{5',Me}$ = 6.1 Hz, 3 H, 5-CH_3), 1.46 [s, 9 H, C(CH_3)$_3$], 1.54, 1.81, 2.10 (3 m, 4 H, 3′-H_A, 3′-H_B, 4′-H_A, 4′-H_B), 4.20 (ddq, $J_{4'A,5'}$ = 6.1, $J_{4'B,5'}$ = 7.6, $J_{5',Me}$ = 6.1 Hz, 1 H, 5′-H), 4.35 (dd, $J_{2,2'}$ = 3.2, $J_{2,NH}$ = 8.2 Hz, 1 H, 2-H), 4.49 (ddd, $J_{2,2'}$ = 3.5, $J_{2',3'A}$ = 6.1, $J_{2',3'B}$ = 8.5 Hz, 1 H, 2′-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$, 323 K): δ = 21.3 (q, 5′-CH_3), 28.6 [q, C(CH_3)$_3$], 29.2, 34.0 (2 t, C-3′, C-4′), 56.9 (d, C-2), 77.2 (d, C-5′), 78.6 (d, C-2′), 80.6 [s, C(CH_3)$_3$], 156.7 (s, NHCO), 174.8 (s, COOH) ppm. $C_{12}H_{21}NO_5$ (259.3): calcd. C 55.58, H 8.17, N 5.40; found C 55.41, H 8.15, N 5.29.

(2*S*,2′*R*,5′*S*)-2-Amino-2-(5′-methyltetrahydrofuran-2′-yl)acetic Acid Hydrochloride, L-Dihydrofuranomycin Hydrochloride (4): This compound was prepared following the procedure described for the preparation of **1**; *N*-Boc-amino acid **33** (196 mg, 0.76 mmol), conc. HCl (2 mL) in methanol/water (4:1, 5 mL); reaction time 16 h at 4 °C. Work up as described above for **1** gave a colourless solid, which was dissolved in water (5 mL). After addition of conc. HCl (1 mL) the crude product was crystallized from water/acetone to yield dihydrofuranomycin hydrochloride (**4**·HCl) as a colourless solid (91 mg, 62%), m.p. 205–207 °C. $[\alpha]_D^{20}$ = +9.63 (*c* = 0.420, CH_3OH). IR (KBr): $\tilde{\nu}$ = 3424 (b), 2972, 2360, 2341, 1750, 1501, 1074 cm^{-1}. ^1H NMR (500.2 MHz, D_2O): δ = 1.13 (d, $J_{5',Me}$ = 6.1 Hz, 3 H, 5-CH_3), 1.65, 1.86, 2.03, 2.12 (4 m, 4 H, 3′-H_A, 3′-H_B, 4′-H_A, 4′-H_A), 3.61 (d, $J_{2,2'}$ = 6.3 Hz, 1 H, 2-H), 4.12 (ddq, $J_{5',Me}$ = 6.1, $J_{4'A,5'}$ = 6.1, $J_{4'B,5'}$ = 7.6 Hz, 1 H, 5′-H), 4.28 (d, $J_{2,2'}$ = 6.3, 1 H, 2′-H) ppm. ^{13}C NMR (75.5 MHz, D_2O): δ = 20.3 (q, 5′-CH_3), 29.2 (t, C-3′), 33.2 (t, C-4′), 56.8 (d, C-2), 76.6 (d, C-2′), 77.8 (d, C-5′), 171.0 (s, COOH) ppm. $C_7H_{14}NO_3Cl$ (195.7): calcd. C 42.96, H 7.22, N 7.16; found C 42.65, H 7.60, N 6.34.

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