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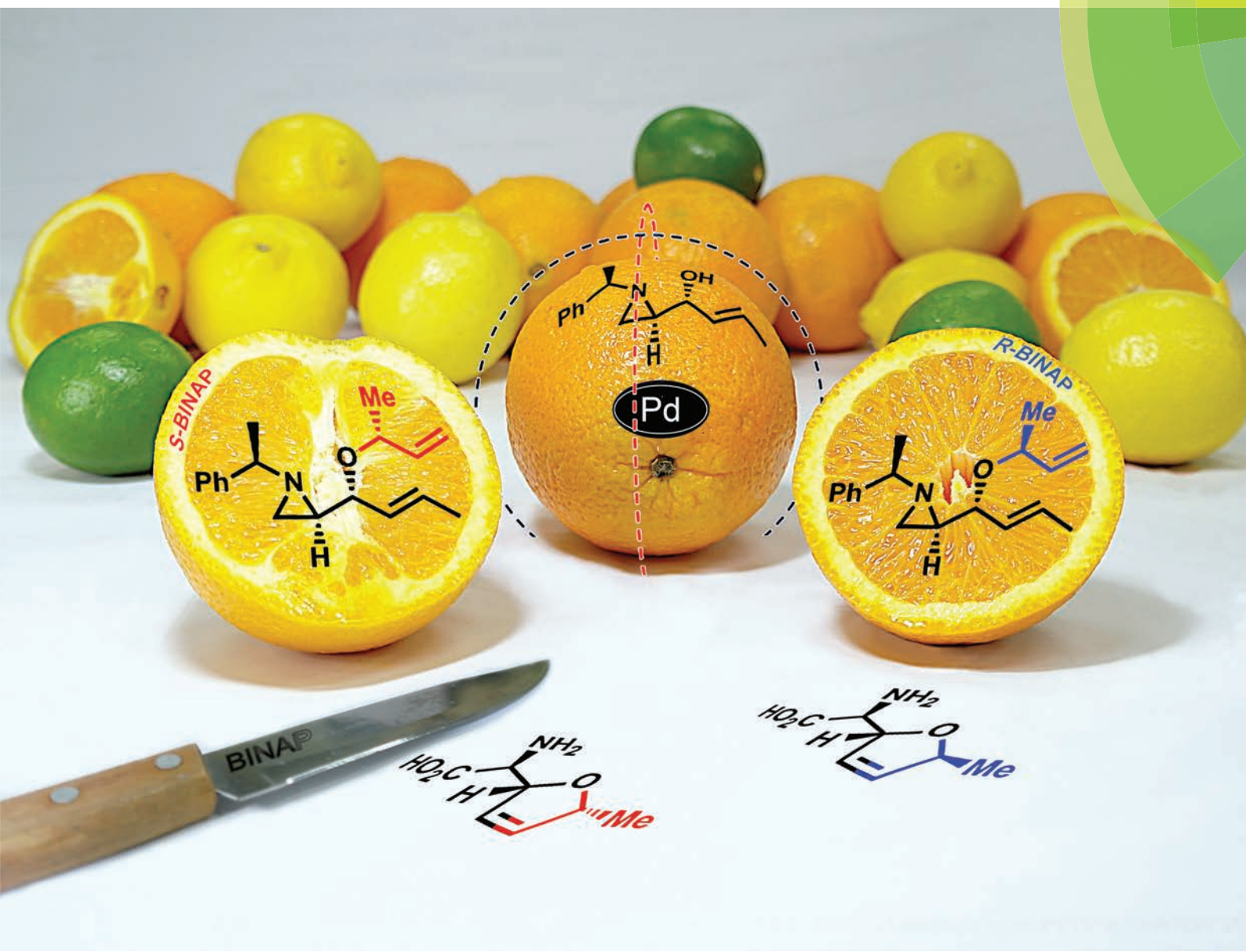


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# Stereoselective Pd-catalyzed etherification and asymmetric synthesis of furanomycin and its analogues from a chiral aziridine†

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A chiral aziridine was utilized for the synthesis of the anti-bacterial natural amino acid L-(+)-furanomycin, and its analogues including 5′-*epi*-furanomycin and norfuranomycin. Key steps of this synthesis are the stereoselective Pd-catalyzed etherification for diallyl ethers and ring closing metathesis.

## Introduction

L-(+)-Furanomycin as a naturally occurring amino acid bearing 3,4-dihydrofuran was isolated from *Streptomyces threomyceticus* in 1967 by Katagiri *et al.* with antibacterial activity against microorganisms such as *E. coli*, *Bacillus subtilis* and several *Salmonella* and *Shigella* strains (MIC 1–5 μg $mL^{-1}$).[1] Furanomycin features a unique structure with the 5-methyl-3,4-dihydrofuran ring whose absolute configuration was fully characterized by X-ray analysis of the *N*-acetyl derivatives (Fig. 1).[2] This unusual amino acid as an antagonist of isoleucine is incorporated into the bacterial protein biosynthesis machinery at the site for isoleucine possibly due to the similarity of their conformations deduced from NMR studies.[3] This type of translatable amino acid possibly yields peptides and proteins containing nonproteogenic amino acids and this is one of the hottest research areas nowadays.[4,5]


**1a** furanomycin ($R^1$ = Me, $R^2$ = H)
**1b** 5′-*epi*-furanomycin ($R^1$ = H, $R^2$ = Me)
**1c** norfuranomycin ($R^1$ = $R^2$ = H)

Isoleucine

**Fig. 1** Structure of furanomycin (**1a**) and its analogues (**1b**, **1c**).

There are a lot of studies detailing the synthesis of furanomycin[1,6] and its analogues,[7] the mechanism of action relating to protein biosynthesis and structure–activity relationships aimed at possible improvements of its antibacterial activity.[8] Many synthetic approaches started from the chiral pool including xylose, dimethyl tartrate, furanose, mannitol and Garner's aldehyde with various reactions in attempts to make the 3,4-dihydrofuran ring.[6,7] Most of the 3,4-dihydrofuran rings next to the amino acid were elaborated by introducing electron-rich furan analogues into the electrophilic carbon or by cyclization of allenic or allylic alcohols.[1a,6,7] Ring-closing metathesis (RCM) of allyl ethers has also been reported for making the 3,4-dihydrofuran ring in high yield using either Grubbs' first or second generation catalyst.[1b,6a,b] To apply this synthetic strategy in building the 3,4-dihydrofuan ring by RCM, one problem still remains to be solved for the generation of allyl ethers as the synthetic precursor in a highly stereoselective manner. As an example, direct etherification of allyl alcohols bearing Garner's aldehyde as the amino acid part with 3-chloro-1-butene yielded almost a 1 : 1 mixture of diastereomers.[7f] A similar ether was also derived in low yield from Ireland–Claisen [3,3]-sigmatropic rearrangement of an allylglycinate as a diastereomeric mixture in 72 : 28 ratio.[6a] In this report we describe the synthesis of L-(+)-furanomycin and its analogues such as 5′-*epi*-furanomycin and norfuranomycin on the basis of RCM of the diallyl ethers which were generated from stereoselective Pd-catalyzed etherification of the branched alkyl part of the requisite ether starting from chiral aziridine-2-carboxylate.

Over the last few years we have shown that the enantiopure aziridine-2-carboxylates are good starting substrates for the asymmetric synthesis of various amino acids.[9] All of these

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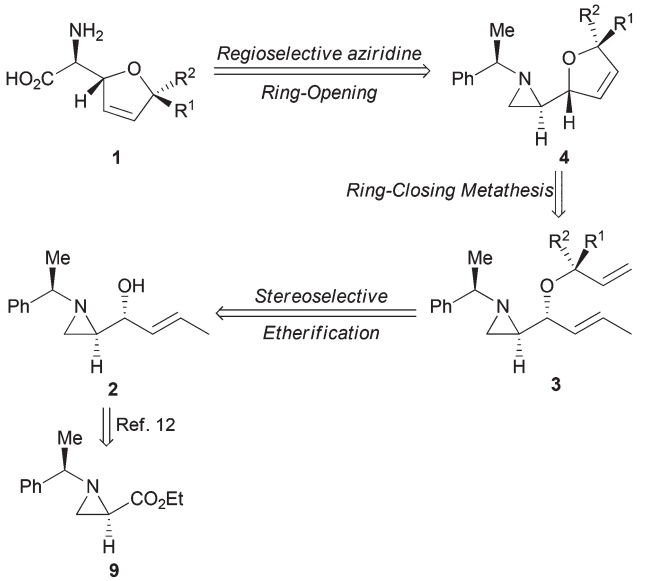
† Electronic supplementary information (ESI) available: $^1$H NMR, $^{13}$C NMR and 2D NMR spectra. See DOI: 10.1039/c5ob00375j

syntheses are based on the functional group transformation of the carboxylate into properly functionalized alkyl or aryl groups. The aziridine ring opening by oxygen nucleophile in a regio- and stereoselective manner affords an amino alcohol which can be oxidized to an amino acid, if necessary.[9,10] Thus the aziridine ring part serves as a synthetic precursor of the corresponding amino alcohol or amino acid which is similar to what the ring part of Garner's aldehyde does.[11] However, aziridine-2-carboxylate is preferred to Garner's aldehyde because the chiral centre of the alcohol next to the aziridine is generated easily either in a *threo* or *erythro* fashion from the selective reduction of 2-acylaziridine derived from aziridine-2-carboxylate with much better stereoselectivity than the compounds from the Garner aldehyde.[12]

Taking advantage of the aforementioned aziridine chemistry we envisioned the synthesis of furanomycin (**1a**), 5′-*epi*-furanomycin (**1b**) and norfuranomycin (**1c**) with retrosynthetic analysis as shown in Scheme 1. Aziridine-2-yl-3′,4′-dihydrofuran ring **4** is quite feasible as a synthetic precursor of furanomycin and its analogues. The aziridine ring may serve as a synthetic precursor of an amino acid by ring opening with a hydroxyl nucleophile to yield an amino alcohol. The amino alcohol can be easily oxidized to yield a carboxylate group for conversion into an α-amino acid. The requisite 3′,4′-dihydrofuran ring can be derived from the diallyl ether **3** *via* ring-closing metathesis. The key synthetic intermediate **3** should be generated by stereoselective etherification of compound **2**. Compound **2** is easily prepared from the stereoselective reduction of 2-acylaziridine originated from (2*S*)-aziridine-2-carboxylate (**9**) with the same configuration as an L-amino acid following our earlier report.[12]




**Scheme 1** Retrosynthetic analysis for the synthesis of furanomycin (**1a**, $R^1$ = Me, $R^2$ = H), 5′-*epi*-furanomycin (**1b**, $R^1$ = H, $R^2$ = Me), and norfuranomycin (**1c**, $R^1$ = H, $R^2$ = H).

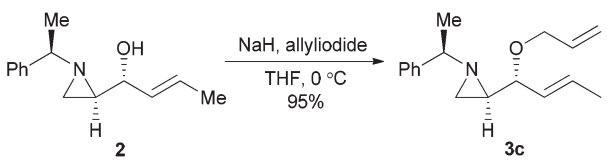
## Results and discussion

We started out with the synthesis of norfuranomycin (**1c**) which has a simple 3′,4′-dihydrofuran ring compared to the furanomycin (**1a**) and 5′-*epi*-furanomycin (**1b**) with a 5′-methyl-3′,4′-dihydrofuran ring. The (2*R*)-aziridine-2-carboxylate as a starting substrate afforded the requisite *threo*-hydroxyalkylaziridine **2** that bears two important stereocenters at the α- and β-positions of the amino acid in furanomycin and its analogues following our earlier reported method.[12] For preparation of the 3′,4′-dihydrofuran ring, allylic etherification of *threo*-hydroxyalkylaziridine **2** with an allyliodide and NaH yielded the diallyl ether **3c** in 95% yield (Scheme 2).

Ring-closing metathesis[13] of the diallyl ether **3c** was performed with Grubbs' 1st generation catalyst to give the bicyclic compound **4c** consisting of the 3′,4′-dihydrofuran ring and aziridine ring as the amino acid synthetic precursor (Scheme 3). To prepare an amino acid moiety of the norfuranomycin (**1c**), we first carried out the aziridine ring opening reaction with $H_2O$ in the presence of $BF_3{\cdot}OEt_2$ as a Lewis acid followed by cyclization to oxazolidine-2-one **5c** with 1,1′-carbonyldiimidazole (CDI) in the presence of 1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU) in 75% yield in two steps.

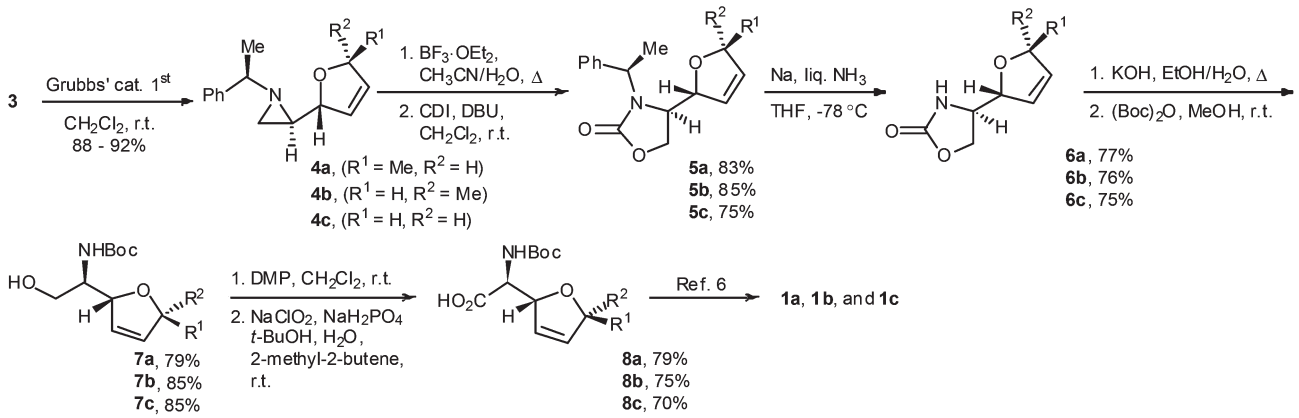
The α-methylbenzyl group of the oxazolidine-2-one **5c** was removed to give **6c** by treatment with Na and liq. $NH_3$ followed by sequential reactions including hydrolysis of the oxazolidine-2-one and Boc-protection to give *N*-Boc-amino alcohol **7c** in 64% yield in two steps. The next and the final step was the oxidation of alcohol **7c** with Dess–Martin periodinane (DMP)[14] followed by $NaClO_2$ to give *N*-Boc-norfuranomycin (**8c**) in high yield. The norfuranomycin (**1c**) could be prepared by *N*-Boc deprotection with trifluoroacetic acid (TFA).[6]

Once we succeeded in synthesizing *N*-Boc norfuranomycin (**8c**) through the formation of the 3′,4′-dihydrofuran ring *via* RCM of an diallyl ether and the generation of an amino acid from the aziridine ring, we decided to apply this synthetic strategy to the syntheses of *N*-Boc protected furanomycin (**8a**) and 5′-*epi*-furanomycin (**8b**). The only difference between these compounds and norfuranomycin is the presence of a methyl group at the 5′-position of the dihydrofuran ring. The configuration of 5′-carbon is "*S*" for furanomycin and "*R*" for 5′-*epi*-furanomcyin. To apply the same synthetic strategy used for the synthesis of norfuranomycin (**1c**), stereoselective etherification of *threo*-hydroxyalkylaziridine **2** with a 3-buten-2-yl halide instead of an allyl iodide is essential to prepare the prerequisite diallyl compounds. Attempts to etherify the aziridinyl alcohol of **2** with 2-halo- or 2-toluenesulfonyloxy-3-butene were




**Scheme 2** Allylic etherification of *threo*-hydroxyalkylaziridine **2**.



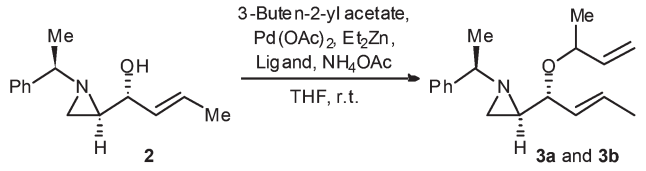

**Scheme 3** Preparation of furanomycin (**1a**), 5′-*epi*-furanomycin (**1b**) and norfuranomycin (**1c**) from diallyl ether **3**.

in vain and did not yield any decent amount of the expected branched diallyl ether. We then applied Lee's method the well-known Pd-catalyzed allylic etherification using an Zn-alkoxide.[15] This protocol stems from "softening" of the alkoxide anion by $Et_2Zn$ which is still nucleophilic enough to make a bond to a Pd-bound allylic cation from 3-buten-2-yl acetate in the presence of a suitable phosphorus ligand.[16] Application of this method in the presence of a phosphorus ligand yielded the expected product **3** as a diastereomeric mixture in moderate yield (Table 1). In most ligands such as $PPh_3$, DPPB and Johnphos, the diastereomeric ratio was about 6 : 4. However, the simple phosphorus ligand $P(OMe)_3$ did not yield any product (Table 1, entry 4). The two diastereomers couldn't be separated and the configuration of the newly formed carbon–oxygen could not be identified.

The same major product was always obtained, even though the ratio was a bit different from phosphorus ligands used in each reaction.

The diastereomeric mixture of **3a** and **3b** could be separated after RCM. To identify the configuration of the major and minor products obtained from Pd-catalyzed allylic etherification, conformationally rigid 5′-methyldihydrofuran fused oxazolidin-2-ones (**5a** and **5b**) obtained through aiziridine ring-opening and oxazolidin-2-one formation were subjected to NOE experiments. As shown in Fig. 2, the methyl proton of the dihydrofuran has correlations with the C5 proton of oxazolidin-2-one for the major diastereomer and with the 2′-proton of dihydrofuran for the minor one. Furthermore, the methyl proton of the dihydrofuran in the major product has a correlation with the phenyl group of the oxazolidin-2-one ring while the minor isomer has correlations between two protons at C5′ of the dihydrofuran ring and C5 of oxazolidin-2-one. Therefore, we found that the major diastereomer has the (*R*)-configuration at the 5′-carbon position which is opposite to the configuration found in the natural isomer of L-(+)-furanomycin.

**Table 1** The Pd-catalyzed allylic etherification from **2** by using $Pd(OAc)_2$ and several phosphorus ligands in the presence of $Et_2Zn$[a]




| Entry | Ligand | Yield | Diastereomeric ratio (**3a** : **3b**)[b] |
|---|---|---|---|
| 1 | $PPh_3$ | 66% | 38 : 62 |
| 2 | DPPB | 65% | 39 : 61 |
| 3 | Johnphos | 82% | 39 : 61 |
| 4 | $P(OMe)_3$ | No reaction | — |

[a] Reaction conditions: 3-buten-2-yl acetate (2.0 equiv.), $Pd(OAc)_2$ (10 mol%), $Et_2Zn$ (0.5 equiv.), ligand (20 mol%), $NH_4OAc$ (1 mol%). [b] The diastereomeric ratio was determined by $^1H$ NMR (400 MHz). DPPB = 1,4-bis(diphenylphosphino)butane, Johnphos = 2-(di-tert-butylphosphino)-biphenyl.

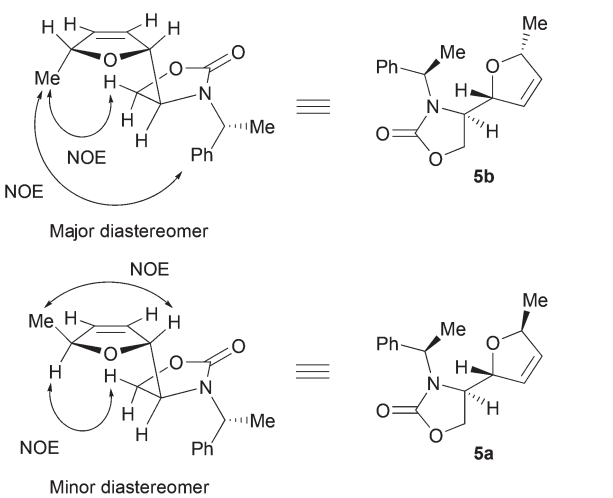
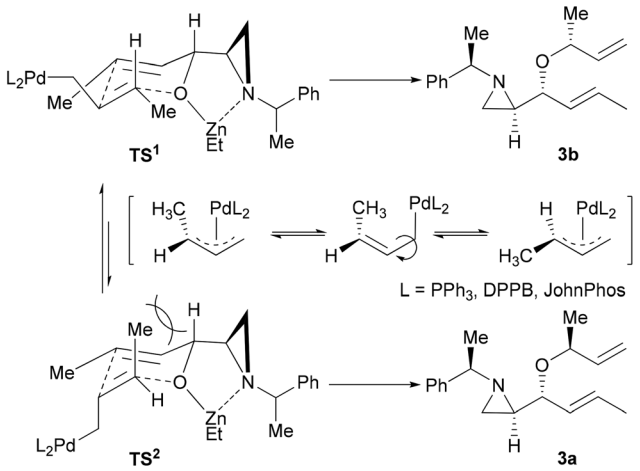



**Fig. 2** Identification of the configuration of two diastereomers by NOE experiments.

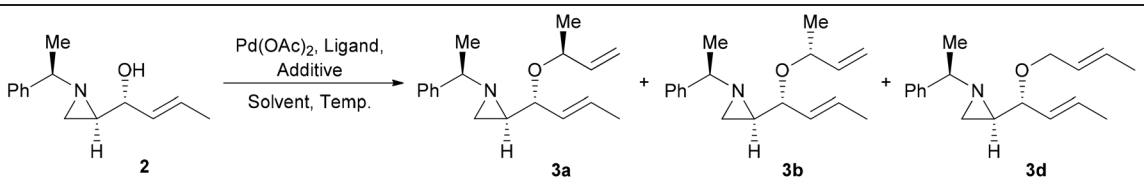



**Scheme 4** The reaction mechanism of the allylic etherification between the allylpalladium complex and Zn-alkoxide.

The proposed reaction mechanism is shown in Scheme 4. First, $\eta^3$-allylpalladium intermediates as soft electrophiles are generated from the racemic allyl acetate and Pd(II). To explain the difference in the stereoselectivity between the major and minor products, $\eta^3$-allylpalladium intermediates must be switchable through fast racemization of the (π-allyl)metal by the $\eta^3$–$\eta^1$–$\eta^3$ step.[17] The next step to discriminate between the two possible diastereomers is to observe how the $\eta^3$-allylpalladium intermediate reacts with an allylic Zn-alkoxide. Zn(II) is bound not only at the oxygen of the allylic alcohol for "softening" of the alkoxide anion but also at the aziridinylamine.[18] When $\eta^3$-allylpalladium intermediates approach the zinc alkoxide, two transition states, $TS^1$ and $TS^2$, are possible. As shown in $TS^1$ for the major **3b**, the $\eta^3$-allylpalladium intermediate approaches the Zn-alkoxide without significant steric strain, while in $TS^2$ the approach to the Zn-alkoxide has a 1,3-diaxial interaction energy to give a minor **3a**.

For the possible enhancement of the stereoselectivity and a switch of the stereochemical outcome to obtain **3a** as the major isomer, we tried Pd-catalyzed etherification with a chiral ligand in the presence of a Zn-alkoxide. When we used (*S*)-BINAP, the reaction yielded the two expected diastereomers **3a** and **3b** in 51% yield and a ratio of 10 : 90. In addition, **3d** originated from the bond formation of the 1° carbon of the isomeric allylpalladium complex with an aziridinyl alcohol was obtained in 7% yield (Table 2, entry 1). After observing the better diastereomeric ratio as 10 : 90 compared to the ratios in Table 1, we decided to switch the chirality of the ligand from (*S*)-BINAP to (*R*)-BINAP (entry 2). (*R*)-BINAP showed a better diastereomeric ratio for the expected isomer as 43 : 57 in 23% yield with a similar amount of **3d**, which showed that the successful switch of the stereochemical pathway was directed by the chirality of the ligand. To improve the reaction yield and the diastereomeric ratio for the natural isomer, the reaction was carried out with a higher amount of $Et_2Zn$ (2.2 equivalents) resulting in a slightly improved ratio of 56 : 44, with **3a**

**Table 2** Optimization of Pd-catalyzed etherification with chiral ligands[a]




| Entry | Ligand | Additive | Solvent | Temp. | Yield | Diastereomeric ratio **3a** : **3b** (isolated yield) | Yield (**3d**) |
|---|---|---|---|---|---|---|---|
| 1[b] | (*S*)-BINAP | $Et_2Zn$ | THF | r.t. | 58% | 10 : 90 (51%) | 7% |
| 2[b] | (*R*)-BINAP | $Et_2Zn$ | THF | r.t. | 23% | 43 : 57 (16%) | 7% |
| 3[b,c] | (*R*)-BINAP | $Et_2Zn$ | THF | r.t. | 28% | 56 : 44 (17%) | 11% |
| 4 | (*R*)-BINAP | $Cs_2CO_3$ | THF | r.t. | N.R. | — | — |
| 5 | (*R*)-BINAP | $Cs_2CO_3$ | THF | 55 °C | N.R. | — | — |
| 6 | (*R*)-BINAP | $Cs_2CO_3$ | $CH_2Cl_2$ | 30 °C | N.D. | — | — |
| 7[d] | (*R*)-BINAP | $Cs_2CO_3$ | $CH_3CN$ | 55 °C | 58% | 67 : 33 (37%) | 21% |
| 8[e] | (*R*)-BINAP | $Cs_2CO_3$ | $CH_3CN$ | 55 °C | 83% | 71 : 29 (54%) | 29% |
| 9[f] | (*R*)-BINAP | $Cs_2CO_3$ | $CH_3CN$ | 55 °C | 81% | 70 : 30 (51%) | 30% |
| 10 | (*R*)-BINAP | $K_2CO_3$ | $CH_3CN$ | 55 °C | 32% | 69 : 31 (22%) | 10% |
| 11[g] | (*R*)-BINAP | $Cs_2CO_3$ | $CH_3CN$ | 55 °C | 26% | 66 : 34 (26%)[h] | — |
| 12 | (*S*,*S*)-DACH-phenyl | $Cs_2CO_3$ | $CH_3CN$ | 55 °C | N.R. | — | — |
| 13 | (*R*,*R*)-DACH-phenyl | $Cs_2CO_3$ | $CH_3CN$ | 55 °C | N.R. | — | — |

[a] Reaction conditions: $Pd(OAc)_2$ (10 mol%), ligand (20 mol%), 3-buten-2-yl-acetate (2.0 equiv.), base (3.0 equiv.). [b] Reaction conditions: $Pd(OAc)_2$ (10 mol%), ligand (20 mol%), 3-buten-2-yl-acetate (2.0 equiv.), $Et_2Zn$ (0.5 equiv.), $NH_4OAc$ (1 mol%). [c] $Et_2Zn$ (2.2 equiv.). [d] The allylpalladium complex was not preformed. [e] 3-Buten-2-yl acetate (5.0 equiv.). [f] 3-Buten-2-yl acetate (1.1 equiv.). [g] 3-Penten-2-yl acetate (1.1 equiv.). [h] The diastereomeric ratio of products from the reaction with 3-penten-2-yl acetate. N.D. = not detectable, N.R. = no reaction, (*S*,*S*)-DACH-phenyl = (1*S*,2*S*)-(−)-1,2-diaminocyclohexane-*N*,*N*′-bis(2-diphenylphosphinobenzoyl); (*S*,*S*)-DACH-phenyl Trost ligand, (*R*,*R*)-DACH-phenyl = (1*R*,2*R*)-(+)-1,2-diaminocyclohexane-*N*,*N*′-bis(2-diphenylphosphinobenzoyl); (*R*,*R*)-DACH-phenyl Trost ligand.

as the major product, in 28% yield (entry 3). Though we were able to get the **3a** isomer as the major product, problems still remained including lower yields of **3a** and **3b** and the formation of significant amounts of **3d**. Therefore, we tried to perform Pd-catalyzed etherification with $Cs_2CO_3$ as a base in the absence of $Et_2Zn$.[19] The reaction with $Cs_2CO_3$ in THF and $CH_2Cl_2$ did not yield any detectable amount of the product (entries 4–6). However, in $CH_3CN$ the reaction yielded the expected products in 58% yield with the diastereomeric ratio of **3a** : **3b** being 67 : 33, while **3d** was also obtained in 21% yield (entry 7). These results proved that **3a** as a major product originated from the change of the stereochemical pathway through the different transition state from those in Scheme 4 without "Zn" bound coordination. To improve the reaction yield, an excess amount of the starting allyl acetate (5.0 equiv.) was used to preform allylpalladium complex more. This resulted in 83% total yield with a slightly improved diastereomeric ratio of 71 : 29 (entry 8). However, the reaction was not sensitive to the amount of the starting acetate. A similar 81% reaction yield was obtained with 1.1 equivalent of 3-buten-2-yl acetate (entry 9). Changing the base from $Cs_2CO_3$ to $K_2CO_3$ decreased the reaction yield dramatically (entry 10).

To eliminate the possible formation of **3d** from the bond formation at the 1° carbon in the allylpalladium complex, we used 3-penten-2-yl acetate instead of 3-buten-2-yl acetate to yield etherification products with a similar diastereomeric ratio of 66 : 34 in 26% yield. Therefore, we carried out the etherification reaction as shown in entry 8 in Table 2 for the next step.

Oxazolidin-2-ones **5a** and **5b** were prepared from **3a** and **3b** *via* ring-closing metathesis and the aziridine ring opening reaction with $H_2O$ followed by cyclization. From the bicyclic compounds **5a** and **5b**, *N*-Boc protected furanomycin (**8a**) and 5′-*epi*-furanomycin (**8b**) were synthesized by following the same procedure used for the synthesis of norfuranomycin (**8c**) and the reaction yields were similar (Scheme 3).

## Conclusions

We achieved syntheses of *N*-Boc protected L-(+)-furanomycin and its analogues including *N*-Boc protected 5′-*epi*-furanomycin and norfuranomycin from the common intermediate *threo*-hydroxyalkylaziridine **2**. Key steps of these syntheses are the stereoselective etherification of *threo*-hydroxyalkylaziridine for diallyl ethers and ring-closing metathesis to form 1′,5′-dihydrofurans. In particular, 5′-methyl-1′,5′-dihydrofuran bearing an extra stereocenter at the 5′-position was prepared from the stereoselective etherification product between the allylpalladium intermediate and *threo*-hydroxyalkylaziridine. Proper selection of the phosphorus ligand and the reaction conditions allowed us to switch the stereochemical outcome of the etherification reaction. An *N*-Boc-protected amino acid was prepared from the aziridine ring *via* regioselective aziridine ring-opening reaction with $H_2O$ and subsequent reactions including oxidation of amino alcohols.

## Experimental

### Materials and methods

Chiral aziridines are available from Aldrich. All commercially available compounds were used as received unless stated otherwise. All reactions were carried out under an atmosphere of nitrogen in oven-dried glassware with a magnetic stirrer. Reactions were monitored by thin layer chromatography (TLC) with 0.25 mm E. Merck pre-coated silica gel plates (60 F254). Visualization was accomplished with either UV light, or by immersion in solutions of ninhydrin, *p*-anisaldehyde, or phosphomolybdic acid (PMA) followed by heating on a hot plate for about 10 s. Purification of reaction products was carried out by flash chromatography using Kieselgel 60 Art 9385 (230–400 mesh). $^1$H-NMR and $^{13}$C-NMR spectra were obtained using a Varian unity lNOVA 400WB (400 MHz) or Bruker AVANCE III HD (400 MHz) spectrometer. Chemical shifts are reported relative to chloroform ($\delta$ = 7.26) for $^1$H NMR and chloroform ($\delta$ = 77.2) for $^{13}$C NMR. Data are reported as (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, p = quintet, m = multiplet). Coupling constants are given in Hz. Ambiguous assignments were resolved on the basis of standard one dimensional proton decoupling experiments. Optical rotations were obtained using a Rudolph Autopol III digital polarimeter and JASCO P-2000. Optical rotation data were reported as follows: $[\alpha]^{20}$ (concentration $c$ = g/100 mL, solvent). High resolution mass spectra were recorded on a 4.7 Tesla IonSpec ESI-TOFMS, JEOL (JMS-700) and AB Sciex 4800 Plus MALDI TOF™ (2,5-dihydroxybenzoic acid (DHB) matrix was used to prepare samples for MS). Data were obtained in the reflector positive mode with internal standards for calibration.

### Synthetic procedure

**(2*R*)-2-((1*R*,*E*)-1-(But-3-en-2-yloxy)but-2-enyl)-1-((*R*)-1-phenylethyl)aziridine (3a, 3b)**

*For synthesis of furanomycin.* To a solution of (*R*,*E*)-1-((*R*)-1-((*R*)-1-phenylethyl)aziridin-2-yl)but-2-en-1-ol **2** (1.02 g, 4.69 mmol) in $CH_3CN$ (44 mL) was added $Cs_2CO_3$ (4.587 g, 14.08 mmol) at room temperature. After 20 min, a solution including but-3-en-2-yl acetate (2.98 mL, 23.47 mmol), $Pd(OAc)_2$ (105 mg, 0.470 mmol), and (*R*)-BINAP (584 mg, 0.939 mmol) in $CH_3CN$ (3 mL) was added to the solution of **2**. The mixture was warmed to 55 °C. After 12 h, the reaction mixture was moved directly onto a silica gel column. The reaction mixture was purified by flash chromatography (1 : 12 = EtOAc : Hex). The **3a**, **3b** mixed product (687 mg, 54%) was obtained as a colorless oil. Compound **3d** was also obtained.

*For synthesis of 5′-epi-furanomycin.* To a solution of (*R*,*E*)-1-((*R*)-1-((*R*)-1-phenylethyl)aziridin-2-yl)but-2-en-1-ol **2** (100 mg, 0.460 mmol) in THF (1 mL) was added dropwise $Et_2Zn$ (0.230 mL, 1.0 M in hexane) *via* a syringe at room temperature. After 30 min, the mixture turned cloudy white. To this suspension were added in one portion but-3-en-2-yl acetate (0.064 mL, 0.506 mmol), $Pd(OAc)_2$ (10 mg, 0.046 mmol), (*S*)-BIANP (57 mg, 0.092 mmol) and $NH_4OAc$ (3 mg, 0.046 mmol) in THF (1 mL) at 0 °C. The solution was stirred for 9 h at room

temperature. The reaction mixture was moved directly onto a silica gel column and purified by flash chromatography (1 : 12 = EtOAc : Hex). The **3a**, **3b** mixed product (63 mg, 51%) was obtained as a colorless oil. Compound **3d** was also obtained.

$^1$H NMR (400 MHz, $CDCl_3$, $Me_4Si$): $\delta$ 7.39–7.21 (5H, m, **3a** and **3b**), 5.79 (1H, ddd, $J$ = 14.7, 10.4, 6.67 Hz, **3a**), 5.78 (1H, ddd, $J$ = 17.2, 10.3, 6.9 Hz, **3b**), 5.71–5.54 (1H, m, **3a** and **3b**), 5.48 (1H, m, **3b**), 5.41 (1H, dddd, $J$ = 15.3, 7.6, 3.1, 1.5 Hz, **3a**), 5.18 (1H, dddd, $J$ = 48.0, 10.5, 1.8, 1.1 Hz, **3a**), 5.16 (1H, dddd, $J$ = 48.3, 10.3, 1.7, 1.0 Hz, **3b**), 4.39 (1H, p, $J$ = 6.5 Hz, **3b**), 4.05 (1H, pt, $J$ = 6.4, 0.9 Hz, **3a**), 3.44 (1H, m, **3a** and **3b**), 2.43 (1H, q, $J$ = 6.6 Hz, **3b**), 2.42 (1H, q, $J$ = 6.5 Hz, **3a**), 1.72 (3H, ddd, $J$ = 6.5, 1.6, 0.5 Hz, **3a**), 1.69 (3H, ddd, $J$ = 6.4, 1.6, 1.0 Hz, **3b**), 1.68–1.63 (1H, m, **3a** and **3b**), 1.49 (1H, d, $J$ = 3.6 Hz, **3a**), 1.48 (3H, d, $J$ = 6.6 Hz, **3b**), 1.46 (3H, d, $J$ = 6.5 Hz, **3a**), 1.44 (1H, d, $J$ = 3.6 Hz, **3b**), 1.29 (3H, d, $J$ = 6.4 Hz, **3b**), 1.25 (3H, d, $J$ = 6.4 Hz, **3a**), 1.24 (1H, d, $J$ = 6.7 Hz, **3a**), 1.23 ppm (1H, d, $J$ = 6.7 Hz, **3b**); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 145.0, 141.2, 141.0, 128.5, 127.1, 127.0, 115.3, 115.2, 79.9, 79.8, 75.2, 73.6, 70.0, 69.9, 44.3, 30.4, 30.3, 23.5, 21.9, 21.5, 18.0, 17.9 ppm; HRMS-MALDI ($m/z$): $[M + H]^+$ calcd for $C_{18}H_{25}NO + H^+$, 272.2009; found, 272.2003.

*Compound* ***3d***. $[\alpha]^{20}$ +56° ($c$ 0.49 in $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$, $Me_4Si$): $\delta$ 7.44–7.22 (5H, m), 5.82–5.59 (3H, m), 5.48 (1H, ddd, $J$ = 14.1, 7.1, 1.2 Hz), 4.05 (2H, m), 3.40 (1H, t, $J$ = 7.5 Hz), 2.46 (1H, q, $J$ = 6.5 Hz), 1.81–1.67 (1H, m), 1.74 (6H, m), 1.52 (4H, m), 1.27 ppm (1H, d, $J$ = 6.3 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 144.8, 135.5, 129.5, 128.8, 128.7, 128.4, 128.3, 127.0, 116.1, 82.3, 70.0, 69.6, 44.3, 30.3, 23.4, 18.0 ppm; HRMS-MALDI ($m/z$): $[M]^+$ calcd for $C_{18}H_{25}NO^+$, 271.1931; found, 271.1933.

**(*R*)-2-((*R*,*E*)-1-(Allyloxy)but-2-enyl)-1-((*R*)-1-phenylethyl)aziridine (3c).** To a solution of (*R*,*E*)-1-((*R*)-1-((*R*)-1-phenylethyl)aziridin-2-yl)but-2-en-1-ol **2** (2.89 g, 13.29 mmol) in THF (50 mL) were added NaH (478 mg, 19.939 mmol) and allyliodide (1.46 mL, 15.95 mmol) at 0 °C and then warmed to room temperature. The resulting mixture was stirred for 3 h and then quenched with aq. $NaHCO_3$. The mixture was extracted with EtOAc. The combined organic layer was washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was purified by silica gel column chromatography (1 : 12 = EtOAc : Hex). The desired product (3.24 g, 95%) as a yellow oil was obtained. $[\alpha]^{20}$ +91° ($c$ 0.81 in $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$, $Me_4Si$): $\delta$ 7.22–7.38 (5H, m), 5.95 (1H, ddt, $J$ = 17.2, 10.5, 5.3 Hz), 5.67 (1H, dqd, $J$ = 15.4, 6.5, 0.9 Hz), 5.46 (1H, ddq, $J$ = 15.4, 7.7, 1.6 Hz), 5.34 (1H, ddd, $J$ = 17.2, 3.6, 1.8 Hz), 5.16 (1H, ddt, $J$ = 10.5, 1.9, 1.4 Hz), 4.09 (2H, dddt, $J$ = 35.7, 13.1, 5.3, 1.6 Hz), 3.39 (1H, t, $J$ = 7.6 Hz), 2.45 (1H, q, $J$ = 6.5 Hz), 1.73 (3H, ddd, $J$ = 6.5, 1.6, 0.5 Hz), 1.67–1.71 (1H, m), 1.52 (1H, d, $J$ = 3.6 Hz), 1.49 (3H, d, $J$ = 6.6 Hz), 1.26 ppm (1H, d, $J$ = 6.7 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 144.8, 135.5, 129.4, 129.0, 128.4, 127.1, 127.0, 116.2, 82.5, 70.00, 69.6, 44.3, 30.4, 23.4, 18.0 ppm; HRMS-ESI ($m/z$): $[M + Na]^+$ calcd for $C_{17}H_{23}NO + Na^+$, 280.1672; found, 280.1677.

**(*R*)-2-((2*R*,5*S*)-5-Methyl-2,5-dihydrofuran-2-yl)-1-((*R*)-1-phenylethyl)aziridine (4a) and (*R*)-2-((2*R*,5*R*)-5-methyl-2,5-dihydrofuran-2-yl)-1-((*R*)-1-phenylethyl)aziridine (4b).** To a solution of (2*R*)-2-((1*R*,*E*)-1-(but-3-en-2-yloxy)but-2-en-1-yl)-1-((*R*)-1-phenylethyl)aziridine **3** (1.52 g, 5.59 mmol) in $CH_2Cl_2$ (56 mL) was added Grubbs' 1$^{st}$ generation catalyst (0.460 g, 0.559 mmol) at room temperature. After 20 h, the reaction mixture was concentrated *in vacuo*. The reaction mixture was purified by column chromatography (1 : 8 to 1 : 5 = EtOAc : Hex). Diastereomeric compounds (**4a** and **4b**, 1.13 g, 88%) as colorless oils were obtained respectively.

*Compound* ***4a***. $[\alpha]^{20}$ +235° ($c$ 1.14 in $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$, $Me_4Si$): $\delta$ 7.39–7.21 (5H, m), 5.88 (1H, ddd, $J$ = 6.1, 2.1, 1.5 Hz), 5.74 (1H, m), 5.05 (1H, m), 4.65 (1H, m), 2.43 (1H, q, $J$ = 6.5 Hz), 1.61 (2H, m), 1.46 (3H, d, $J$ = 6.6 Hz), 1.27 (3H, d, $J$ = 6.4 Hz), 1.25 ppm (1H, d, $J$ = 6.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 144.9, 133.3, 128.4, 127.1, 127.0, 127.0 87.5, 82.3, 69.8, 43.3, 29.8, 23.6, 22.0 ppm; HRMS-MALDI ($m/z$): $[M + H]^+$ calcd for $C_{15}H_{19}NO + H^+$, 230.1539; found, 230.1532.

*Compound* ***4b***. $[\alpha]^{20}$ +83° ($c$ 1.05 in $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$, $Me_4Si$): $\delta$ 7.22–7.40 (5H, m), 5.86 (1H, ddd, $J$ = 6.1, 2.3, 1.4 Hz), 5.73 (1H, m), 4.92–4.98 (1H, m), 4.51 (1H, dddd, $J$ = 7.1, 3.6, 2.2, 1.5 Hz), 2.44 (1H, q, $J$ = 6.5 Hz), 1.62 (1H, d, $J$ = 3.5 Hz), 1.56 (1H, td, $J$ = 6.7, 3.5 Hz), 1.47 (3H, d, $J$ = 6.6 Hz), 1.34 (3H, d, $J$ = 6.4 Hz), 1.27 ppm (1H, d, $J$ = 6.5 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 144.9, 133.3, 128.4, 127.1, 127.0, 126.9, 88.2, 82.4, 69.8, 44.4, 30.0, 23.6, 23.2 ppm; HRMS-MALDI ($m/z$): $[M + H]^+$ calcd for $C_{15}H_{19}NO + H^+$, 230.1539; found, 230.1534.

**(*R*)-2-((*R*)-2,5-Dihydrofuran-2-yl)-1-((*R*)-1-phenylethyl)aziridine (4c).** The product was obtained using the same procedure as that for the synthesis of **4a** and **4b**. The desired product (92%) as a colorless oil was obtained; $[\alpha]^{20}$ +121° ($c$ 0.015 in $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$, $Me_4Si$): $\delta$ 7.39–7.22 (5H, m), 5.99 (1H, ddt, $J$ = 6.3, 2.2, 1.6 Hz), 5.78 (1H, dtd, $J$ = 6.3, 2.4, 1.5), 4.76 (1H, dddd, $J$ = 12.8, 6.0, 2.4, 1.6 Hz), 4.66 (1H, dddd, $J$ = 12.8, 4.0, 2.5, 1.6 Hz), 4.58 (1H, m), 2.44 (1H, q, $J$ = 6.5 Hz), 1.63 (1H, d, $J$ = 3.5 Hz), 1.62 (1H, m), 1.47 (3H, d, $J$ = 6.6 Hz), 12.8 ppm (1H, d, $J$ = 6.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 144.8, 128.4, 128.3, 127.4, 127.1, 127.0, 88.3, 75.7, 69.8, 43.2, 29.8, 23.6 ppm; HRMS-ESI ($m/z$): $[M + Na]^+$ calcd for $C_{14}H_{17}NO + Na^+$, 238.1202; found, 238.1206.

**(*R*)-4-((2*R*,5*S*)-5-Methyl-2,5-dihydrofuran-2-yl)-3-((*R*)-1-phenylethyl)oxazolidin-2-one (5a), (*R*)-4-((2*R*,5*R*)-5-methyl-2,5-dihydrofuran-2-yl)-3-((*R*)-1-phenylethyl)oxazolidin-2-one (5b) and (*R*)-4-((*R*)-2,5-dihydrofuran-2-yl)-3-((*R*)-1-phenylethyl)oxazolidin-2-one (5c).** A solution of the corresponding (*R*)-2-((2*R*,5*S*)-5-methyl-2,5-dihydrofuran-2-yl)-1-((*R*)-1-phenylethyl)-aziridine **4a** (570 mg, 2.49 mmol) and $BF_3{\cdot}OEt_2$ (4.92 mL, 4.48 mmol) in $CH_3CN/H_2O$ = 7 : 1 (62 mL) was refluxed for 3 h. Then, the reaction mixture was hydrolyzed with satd. $NaHCO_3$ (10 mL) and extracted with $Et_2O$ (3 × 30 mL). The combined organic layers were dried with anhydrous $Na_2SO_4$, filtered and concentrated *in vacuo*. The obtained crude product was dissolved in $CH_2Cl_2$ (62 mL), and then 1,1′-carbonyldiimidazole (967 mg, 5.97 mmol) and DBU (1.11 mL, 7.46 mmol) were added to the solution. The reaction mixture was stirred at room temperature

for 12 h. The mixture was extracted with $CH_2Cl_2$. The combined organic layer was washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude compound was purified by column chromatography (1 : 5 = EtOAc : Hex). The product **5a** (564 mg, 83%) as a white powder was obtained.

*Compound **5a**.* Mp 87–90 °C; $[\alpha]^{20}$ +231° (*c* 6.10 in $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$, $Me_4Si$): $\delta$ 7.49–7.25 (5H, m), 5.88 (1H, m), 5.27 (1H, m), 5.20 (1H, q, *J* = 7.2 Hz), 4.89 (1H, m), 4.49 (1H, ddd, *J* = 5.9, 3.7, 1.6 Hz), 4.17 (1H, dd, *J* = 12.5, 4.4 Hz), 3.99 (2H, m), 1.73 (3H, d, *J* = 7.2 Hz), 1.13 ppm (3H, d, *J* = 6.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 158.5, 141.4, 135.6, 128.9, 128.2, 127.5, 123.8, 84.6, 83.5, 63.3, 56.3, 52.2, 21.8, 16.5 ppm; HRMS-MALDI (*m*/*z*): $[M + Na]^+$ calcd for $C_{16}H_{19}NO_3$ + $Na^+$, 296.1257; found, 296.1252.

*Compound **5b**.* The product was obtained in the same manner as **5a**. The desired product (85%) as a white powder was obtained; mp 133–134 °C; $[\alpha]^{20}$ +85° (*c* 0.755 in $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$, $Me_4Si$): $\delta$ 7.47–7.27 (5H, m), 5.83 (1H, m), 5.31 (1H, m), 5.21 (1H, q, *J* = 7.2 Hz), 4.78 (1H, m), 4.39 (1H, ddd, *J* = 6.4, 4.3, 2.0 Hz), 4.18 (1H, t, *J* = 8.8 Hz), 4.11 (1H, dd, *J* = 8.9, 4.5 Hz), 3.96 (1H, dt, *J* = 8.7, 4.4 Hz), 1.74 (3H, d, *J* = 7.2 Hz), 1.23 ppm (3H, d, *J* = 6.5 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 158.5, 141.4, 135.4, 128.8, 128.2, 127.4, 124.1, 85.1, 82.7, 63.4, 55.9, 52.2, 21.5, 16.5 ppm; HRMS-MALDI (*m*/*z*): $[2M + Na]^+$ calcd for $C_{32}H_{38}NO_6$ + $Na^+$, 569.2622; found, 569.2621.

*Compound **5c**.* The procedure was the same as that for the synthesis of **5a**. Purification of the mixture was performed by column chromatography (1 : 3 = EtOAc : Hex). The desired product (75%) as a crystalline solid was obtained; mp 53–54 °C; $[\alpha]^{20}$ +174° (*c* 0.029 in $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$, $Me_4Si$): $\delta$ 7.48–7.27 (5H, m), 5.97 (1H, m), 5.30 (1H, m), 5.23 (1H, q, *J* = 7.2 Hz), 4.60 (1H, dddd, *J* = 13.1, 6.2, 2.4, 1.6 Hz), 4.51 (1H, dddd, *J* = 13.1, 4.2, 2.5, 1.6 Hz), 4.40 (1H, m), 4.17 (1H, td, *J* = 8.4, 0.5 Hz), 4.02 (1H, m), 3.97 (1H, dd, *J* = 8.5, 4.1 Hz), 1.73 ppm (3H, d, *J* = 7.2 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 158.5, 141.3, 130.6, 128.8, 128.3, 127.5, 124.2, 85.2, 76.5, 63.2, 56.1, 52.1, 16.4 ppm; HRMS-ESI (*m*/*z*): $[M + Na]^+$ calcd for $C_{15}H_{17}NO_3$ + $Na^+$, 282.1101; found, 282.1104.

**(*R*)-4-((2*R*,5*S*)-5-Methyl-2,5-dihydrofuran-2-yl)oxazolidin-2-one (6a), (*R*)-4-((2*R*,5*R*)-5-methyl-2,5-dihydrofuran-2-yl)oxazolidin-2-one (6b) and (*R*)-4-((*R*)-2,5-dihydrofuran-2-yl)oxazolidin-2-one (6c).** To a solution of the starting material (*R*)-4-((2*R*,5*S*)-5-methyl-2,5-dihydrofuran-2-yl)-3-((*R*)-1-phenylethyl)oxazolidin-2-one **5a** (565 mg, 2.067 mmol) in THF (21 mL) was added Na (142 mg, 6.20 mmol) at −78 °C under $N_2$. Liquid $NH_3$ was added to the solution until it converted to a dark blue solution and then it was stirred for 30 min. The mixture was quenched with cold water and then extracted with EtOAc (3 × 70 mL). The combined organic mixture was washed with brine (50 mL), dried over $MgSO_4$ and concentrated under vacuum. The product **6a** (269 mg, 77%) as a white powder was obtained.

*Compound **6a**.* Mp 53–54 °C; $[\alpha]^{20}$ +162° (*c* 3.28 in $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 6.04 (1H, ddd, *J* = 6.2, 2.0, 1.5 Hz), 5.68 (1H, m), 5.61 (1H, s), 4.99 (1H, m), 4.86 (1H, ddd, *J* = 7.6, 3.8, 1.8 Hz), 4.43 (1H, t, *J* = 8.7 Hz), 4.30 (1H, dd, *J* = 8.7, 4.9 Hz), 3.83 (1H, ddd, *J* = 8.8, 4.7, 0.6 Hz), 1.26 ppm (3H, d, *J* = 6.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 159.9, 136.2, 124.0, 86.3, 83.2, 66.7, 55.7, 21.8 ppm; HRMS-MALDI (*m*/*z*): $[M + Na]^+$ calcd for $C_8H_{11}NO_3$ + $Na^+$, 192.0631; found, 192.0636.

*Compound **6b**.* The product was obtained in the same manner as **6a**. The desired product (76%) as a white powder was obtained; mp 101–105 °C; $[\alpha]^{20}$ −51° (*c* 0.11 in $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$, $Me_4Si$): $\delta$ 6.01 (1H, ddd, *J* = 6.2, 2.3, 1.4 Hz), 5.66 (1H, ddd, *J* = 6.2, 2.1, 1.6 Hz), 5.64 (1H, bs), 4.97 (1H, m), 4.80 (1H, tdd, *J* = 4.0, 2.3, 1.5 Hz), 4.45 (1H, t, *J* = 8.7 Hz), 4.33 (1H, dd, *J* = 8.7, 4.8 Hz), 3.85 (1H, ddd, *J* = 8.9, 4.8, 0.6 Hz), 1.29 ppm (3H, d, *J* = 6.5 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 159.8, 136.0, 124.0, 86.9, 83.0, 66.7, 55.7, 22.0 ppm; HRMS-MALDI (*m*/*z*): $[M + Na]^+$ calcd for $C_8H_{11}NO_3$ + $Na^+$, 192.0631; found, 192.0632.

*Compound **6c**.* The product was obtained in the same manner as **6a**. Purification of the crude product was performed through recrystalization with 30% DCM in hexane. The desired product (75%) as a white powder was obtained; mp 75–76 °C; $[\alpha]^{20}$ +79° (*c* 0.011 in $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$, $Me_4Si$): $\delta$ 6.22 (1H, s), 6.16 (1H, ddd, *J* = 6.2, 3.7, 1.7 Hz), 5.73 (1H, dtd, *J* = 6.4, 2.5, 1.5 Hz), 4.84 (1H, m), 4.69 (2H, m), 4.44 (1H, t, *J* = 8.7 Hz), 4.30 (1H, dd, *J* = 8.7, 4.9 Hz), 3.89 ppm (1H, ddd, *J* = 8.8, 4.7, 0.6 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 160.2, 131.1, 124.3, 86.7, 76.3, 66.6, 55.6 ppm; HRMS-MALDI (*m*/*z*): $[M + Na]^+$ calcd for $C_7H_9NO_3$ + $Na^+$, 178.0474; found, 178.0477.

***tert*-Butyl ((*R*)-2-hydroxy-1-((2*R*,5*S*)-5-methyl-2,5-dihydrofuran-2-yl)ethyl)carbamate (7a), *tert*-butyl ((*R*)-2-hydroxy-1-((2*R*,5*R*)-5-methyl-2,5-dihydrofuran-2-yl)ethyl)carbamate (7b) and *tert*-butyl (1*R*)-1-(2,5-dihydrofuran-2-yl)-2-hydroxyethylcarbamate (7c).** To a solution of (*R*)-4-((2*R*,5*S*)-5-methyl-2,5-dihydrofuran-2-yl)oxazolidin-2-one **6a** (23.4 mg, 0.138 mmol) in 5 mL of 30% aqueous EtOH was added KOH (23 mg, 0.415 mmol). The mixture was refluxed for 2 h and cooled to room temperature. The reaction mixture was concentrated *in vacuo*. The mixture was neutralized with 0.5 M HCl and then purified using cation exchange resin (Dowex® 50WX2 hydrogen form). The obtained amino alcohol was dissolved in MeOH (2 mL). To the solution was added $(Boc)_2O$ (4.53 mg, 0.207 mmol) at r.t. for 3 h. The solvent was removed *in vacuo*. The crude product was purified by silica gel flash chromatography (1 : 3 to 1 : 1 = EtOAc : Hex). The product **7a** (33.6 mg, 79%) as a colorless oil was obtained.

*Compound **7a**.* $[\alpha]^{20}$ +195° (*c* 2.94 in $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$, $Me_4Si$): $\delta$ 5.82 (2H, dd, *J* = 41.2, 5.7 Hz), 5.08 (1H, d, *J* = 4.4 Hz), 5.01 (2H, dt, *J* = 12.1, 6.1 Hz), 3.88 (1H, d, *J* = 7.1 Hz), 3.74 (2H, m), 2.88 (1H, s), 1.42 (9H, s), 1.24 ppm (3H, d, *J* = 6.3 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 156.5, 132.8, 127.0, 87.5, 83.3, 79.5, 64.8, 54.2, 28.5, 21.9 ppm; HRMS-MALDI (*m*/*z*): $[M + Na]^+$ calcd for $C_{12}H_{21}NO_4$ + $Na^+$, 266.1363; found, 266.1366.

*Compound **7b**.* The product was obtained in the same manner as **7a**. The desired product (85%) as a colorless oil was obtained; $[\alpha]^{20}$ +93° (*c* 4.910 in $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$, $Me_4Si$): $\delta$ 5.79 (2H, dd, *J* = 18.8, 5.8 Hz), 5.02 (2H, br s),

4.93 (1H, m), 3.88 (1H, dd, $J$ = 10.7, 2.0 Hz), 3.76 (2H, m), 2.82 (1H, d, $J$ = 5.5 Hz), 1.42 (9H, s), 1.31 ppm (3H, d, $J$ = 6.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 156.4, 132.5, 127.5, 88.6, 82.7, 79.5, 65.1, 53.2, 28.5, 22.2 ppm; HRMS-MALDI ($m/z$): $[M + Na]^+$ calcd for $C_{12}H_{21}NO_4 + Na^+$, 266.1363; found, 266.1362.

*Compound* ***7c***. The product was obtained in the same manner as **7a**. The desired product (85%) as a colorless oil was obtained; $[\alpha]^{20}$ +181° (*c* 0.84 in $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$, $Me_4Si$): $\delta$ 5.97 (1H, ddd, $J$ = 6.1, 3.6, 1.6 Hz), 5.81 (1H, m), 5.03 (1H, m), 4.71 (1H, dddd, $J$ = 12.7, 6.0, 2.3, 1.7 Hz), 4.62 (1H, dddd, $J$ = 12.7, 4.2, 2.5, 1.6 Hz), 3.81 (1H, m), 3.77 (2H, m), 2.82 (1H, d, $J$ = 6.8 Hz), 1.42 ppm (9H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 156.5, 127.8, 127.5, 88.3, 79.6, 76.3, 64.9, 54.1, 28.5 ppm; HRMS-MALDI ($m/z$): $[M + Na]^+$ calcd for $C_{11}H_{19}NO_4 + Na^+$, 252.1206; found, 252.1200.

**(*S*)-2-((*tert*-Butoxycarbonyl)amino)-2-((2*R*,5*S*)-5-methyl-2,5-dihydrofuran-2-yl)acetic acid (8a), (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-((2*R*,5*R*)-5-methyl-2,5-dihydrofuran-2-yl)acetic acid (8b) and (2*S*)-2-(*tert*-butoxycarbonylamino)-2-(2,5-dihydrofuran-2-yl)acetic acid (8c).** The *tert*-butyl ((*R*)-2-hydroxy-1-((2*R*,5*S*)-5-methyl-2,5-dihydrofuran-2-yl)ethyl)carbamate **7a** (210 mg, 0.862 mmol) was dissolved in $CH_2Cl_2$ (3 mL). Dess–Martin periodinane (475 mg, 1.12 mmol) was added. The mixture was stirred for 1 h, diluted with ether (10 mL), quenched with 10 mL of satd. $Na_2S_2O_3$, and diluted with additional 10 mL of ether. The aqueous phase was extracted with ether (2 × 20 mL), and the combined organic layer was washed with satd. $NaHCO_3$ and brine, then dried with $MgSO_4$ and concentrated under reduced pressure. The obtained *N*-Boc furanomycinal as a yellow oil was carried on to the next step without delay. The crude aldehyde was dissolved in *t*-BuOH (16 mL). Into this solution were added 2-methyl-2-butene (0.958 mL, 9.05 mmol) and $NaH_2PO_4$ (186 mg, 1.55 mmol) in $H_2O$ (2 mL). The stirred mixture was cooled to 0 °C, and $NaClO_2$ (155 mg, 1.72 mmol) in $H_2O$ (1 mL) was added slowly. The mixture was allowed to warm to room temperature and stirred until the reaction solution turned orange-brown. The solvent was evaporated and then the reaction mixture was separated between EtOAc (10 mL) and satd. $NaHCO_3$. The aqueous layer was washed with EtOAc (2 × 10 mL) and was acidified with 1 M HCl to pH 2–3. This solution was extracted with $CH_2Cl_2$ (3 × 20 mL). Combined organic layers were dried with anhydrous $MgSO_4$ and concentrated *in vacuo*. The product **8a** (175 mg, 79%) as a colorless solid was obtained.

*Compound* ***8a***. Mp 151–152 °C (lit.,[1a] 151–153 °C); $[\alpha]^{20}$ +181° (*c* 2.05 in $CHCl_3$) (lit.,[1a] +181° (*c* 1.49 in $CHCl_3$)); $^1$H NMR (400 MHz, $CDCl_3$, $Me_4Si$): $\delta$ 5.91 (1H, d, $J$ = 6.3 Hz), 5.77 (1H, d, $J$ = 6.0 Hz), 5.41 (1H, m), 5.23 (1H, d, $J$ = 9.1 Hz), 5.05 (1H, m), 4.49 (1H, dd, $J$ = 9.2, 1.6 Hz), 1.42 (9H, s), 1.25 ppm (3H, d, $J$ = 6.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 174.5, 156.1, 133.8, 125.9, 86.4, 83.7, 80.2, 56.9, 28.4, 21.8 ppm; HRMS-MALDI ($m/z$): $[M + Na]^+$ calcd for $C_{12}H_{19}NO_5 + Na^+$, 280.1155; found, 280.1158.

*Compound* ***8b***. The product was obtained in the same manner as **7a**. The desired product (75%) as a colorless solid was obtained; mp 96–98 °C (lit.,[1a] 95–100 °C); $[\alpha]^{20}$ +86° (*c* 0.36 in $CHCl_3$) (lit.,[1a] +91.5° (*c* 1.47 in $CHCl_3$)); $^1$H NMR (400 MHz, $CDCl_3$, $Me_4Si$): $\delta$ 7.07 (1H, br s), 5.86 (1H, d, $J$ = 5.6 Hz), 5.76 (1H, d, $J$ = 5.6 Hz), 5.35 (1H, s), 5.16 (1H, d, $J$ = 9.1 Hz), 4.95 (1H, m), 4.53 (1H, d, $J$ = 9.0 Hz), 1.43 (9H, s), 1.32 ppm (3H, d, $J$ = 6.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 174.7, 155.9, 133.4, 126.3, 87.0, 82.9, 80.2, 56.0, 28.4, 22.0 ppm; HRMS-MALDI ($m/z$): $[M + Na]^+$ calcd for $C_{12}H_{19}NO_5 + Na^+$, 280.1155; found, 280.1157.

*Compound* ***8c***. The product was obtained in the same manner as **7a**. The desired product (70%) as a glass-like viscous liquid was obtained; $[\alpha]^{20}$ +100° (*c* 0.56 in $CHCl_3$) (lit.,[7a] enantiomer, −100° (*c* 1.00 in $CHCl_3$)); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 6.04 (1H, d, $J$ = 5.0 Hz), 5.83 (1H, d, $J$ = 4.8 Hz), 5.38 (1H, s) 5.20 (1H, d, $J$ = 9.0 Hz), 4.74 (1H, dd, $J$ = 12.6, 5.6 Hz), 4.65 (1H, m), 4.55 (1H, d, $J$ = 8.0 Hz), 1.44 ppm (9H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 174.7, 156.1, 128.9, 126.3, 86.9, 80.3, 76.6, 56.8, 28.4 ppm; HRMS-MALDI ($m/z$): $[M + Na]^+$ calcd for $C_{11}H_{17}NO_5 + Na^+$, 266.0999; found, 266.0998.

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