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Stereoselective Synthesis of 5-*O*-Carbamoylpolyoxamic Acid by [2,3]-Wittig-Still Rearrangement

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Abstract: Stereoselective [2,3]-Wittig rearrangement of *E*- and *Z*-allylic stannyl ethers derived from an isopropylidene L-threitol derivative has been investigated. The *E*-isomer exhibited best diastereoselectivity and the resulting rearrangement product has been converted to protected polyoxamic acid, an amino acid component of many bioactive polyoxins.

Key words: amino acids and derivatives, carbamates rearrangement, stereoselection, tin and compounds

Introduction

Stereocontrolled carbon-carbon bond formation by [2,3]-Wittig-Still rearrangement is of considerable interest in organic synthesis.[1] We recently examined the level of stereoselectivity associated with this rearrangement for *E*- and *Z*-allylic stannyl ethers derived from an isopropylidene D-ribose derivative.[2] While the *E*-allylic stannyl ether exhibited high diastereoselectivity, the reaction of the *Z*- isomer proceeded with near complete *syn* selectivity. Subsequently, we have utilized this reaction in a stereoselective synthesis of thymine polyoxin C.[2] As part of our synthetic interest in bioactive polyoxins and polyoxamic acid, we have now investigated [2,3]-Wittig rearrangement of *E*- and *Z*-allylic stannyl ethers derived from isopropylidene L-threitol derivative. Herein we report that the rearrangement of the *E*-isomer proceeded with higher diastereoselectivity than the *Z*-isomer and the major isomer has been converted to 5-*O*-carbamoylpolyoxamic acid which is an amino acid component of many bioactive polyoxins.[3] Interests in chemistry and biology led to a number of syntheses of polyoxamic acid derivatives over the years.[4,5]

Results and Discussion

For our investigation of [2,3]-Wittig-Still rearrangement, the required *E*- and *Z*-allylic alcohols **2** and **3** were prepared from the isopropylidene L-threitol derivative **1**.[6] The *E*-alcohol **2** was prepared by Swern oxidation of **1** followed by Horner-Emmons olefination of the resulting aldehyde with triethyl phosphonoacetate and subsequent reduction of the corresponding *trans*-α,β-unsaturated ester with Dibal as described previously.[4j] The *Z*-alcohol was prepared selectively by utilizing Still's variant of Horner-Emmons olefination with bis-(2,2,2-trifluoroethyl)methoxycarbonylmethyl phosphonate[6] followed by Dibal reduction of the resulting *cis*-α,β-unsaturated ester. The alcohols **2** and **3** were treated with potassium hydride and $n\mathrm{Bu_3SnCH_2I}$ in the presence of a catalytic amount of $n\mathrm{Bu_4N^+I^-}$ to furnish the respective *E*- and *Z*-stannyl ethers **4** and **5** (Scheme 1). Subjection

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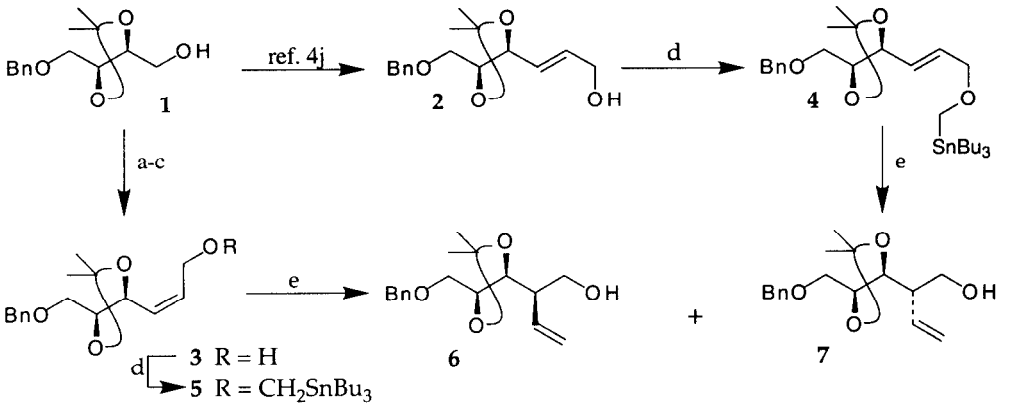
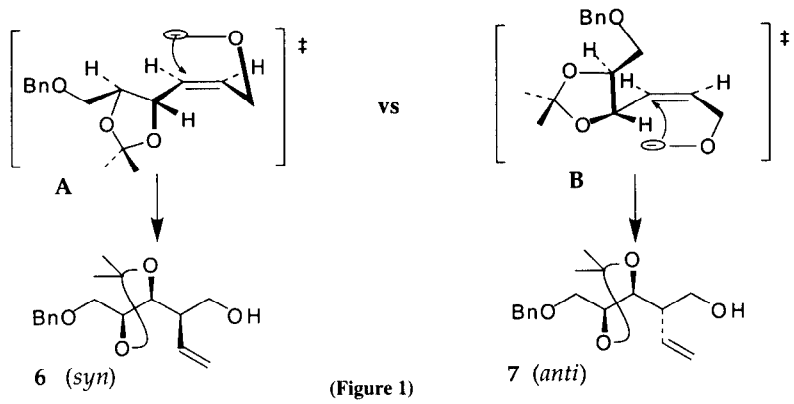
Scheme 1[a]



[a]Key : (a) DMSO, $(COCl)_2$, CH_2Cl_2, -50°C, 2 h then Et_3N; (b) $KN(TMS)_2$, 18-crown-6 $(CF_3CH_2O)_2P(O)CH_2CO_2Me$, THF, -78°C; (c) Dibal, CH_2Cl_2, -78°C, 2 h (60% from 1); (d) KH, n-$Bu_4N^+I^-$, n-Bu_3SnCH_2I, THF, 23°C, 4 h; (e) n-BuLi, THF, -78°C, 2 h (73-81%).

of *E*-stannyl ether **4** to tin-lithium exchange with *n*BuLi at -78°C in THF resulted in a facile [2,3]-rearrangement. An inseparable *syn/anti* mixture (5.4:1 by 400 MHz ^{1}H-NMR) of rearranged products **6** and **7** were isolated in 81% yield after silica gel chromatography. Exposure of the *Z*-stannyl ether **5** to *n*BuLi afforded a mixture (2:1 ratio) of **6** and **7** in 73% yield. While both *E*- and *Z*-stannyl ethers **4** and **5** afforded the *syn*-isomer **6** as the major product, the lack of stereoselectivity for the rearrangement of *Z*-stannyl ether **5** is particularly noteworthy.

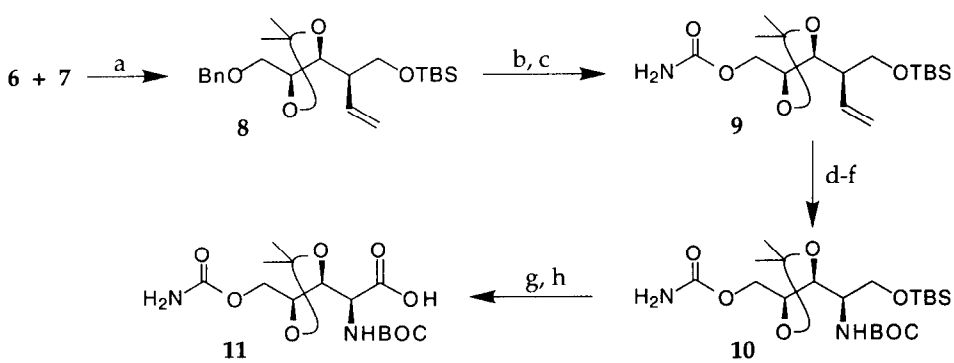
The stereochemical assignment was initially made based upon previous studies of [2,3]-Wittig-Still rearrangement of various stannyl ethers containing an allylic stereocenter.[2,7] Subsequent conversion of the *syn*-isomer **6** to 5-*O*-carbamoylpolyoxamic acid **11** has provided further evidence of this stereochemical assignment. The lack of stereoselectivity for the *Z*-stannyl ether **5** is presumably due to competing transition states **A** and **B** (figure 1). In electronically favored "Houk-like" model **A**, the allylic C-O bond is orthogonal to the plane of allylic C=C and is antiperiplanar with respect to the impending carbanion.[8] The major *syn*-isomer **6** is most likely formed through transition state **A**. In diastereomeric transition state **B**, the allylic substituent is antiperiplanar with respect to the impending carbanion and orthogonal to the plane of C=C bond.[7a] For a larger allylic substitutent, the transition state **B** becomes sterically favorable since it minimizes developing steric interactions. Furthermore, it should be kept in mind that the actual rearrangement substrate is an organolithium species and not an isolated anion. Therefore, possibilities exist that the lithium cation involves in a specific chelation with the acetonide oxygen thereby stabilizing the transition state **B**. To probe this notion, we have carried out 2,3-rearrangement of *Z*-isomer **5** in the presence of pre-complexed *n*BuLi (1.2 equiv) with HMPA (5 equiv) at -78°C in THF. However, the diastereoselectivity of the rearranged products **6** and **7** (2.7:1 by 400 MHz ^{1}H-NMR) was basically unchanged and the product yield was poor (40%). Furthermore, pre-complexed *n*BuLi (1.2 equiv) with TMEDA (4 equiv) at -78°C within 1 h provided 1.7:1 *syn/anti* ratio in 59% yield.[9]



(Figure 1)

For the synthesis of 5-*O*-carbamoylpolyoxamic acid, the mixture of rearranged alcohols **6** and **7** (from **4**) were treated with TBDMSCl and imidazole in DMF to provide the *tert*-butyldimethylsilyl ether **8** in 77% yield after silica gel chromatography. To append the carbamate functionality, the benzyl group was first removed by exposure of **8** to lithium in liquid ammonia. Reaction of the resulting alcohol with *p*-nitrophenylchloroformate in pyridine afforded the mixed carbonate which upon treatment with aqueous ammonia at 0°C for 30 min, furnished the carbamate **9** in 88% yield.[10] The vinyl group in **9** was then transformed into the protected amine functionality in following sequence of steps. Ozonolytic cleavage of the terminal olefin afforded aldehyde which was oxidized with sodium chlorite to the corresponding acid. Curtius rearrangement of the resulting carboxylic acid by exposure to diisopropylethylamine, methylchloroformate and sodium azide at 0°C followed by heating the

Scheme 2[a]



[a]Key : (a) TBDMSCl, imidazole, DMF, 23°C (77%); (b) Li, NH_3; (c) *p*-NO_2-Ph-OCOCl, Py, 0°C, then NH_4OH, THF, 0°C, 30 min (88%); (d) O_3, CH_2Cl_2-MeOH, -78°C then Me_2S, -78° to 23°C; (e) $NaClO_2$, Me_2C=CHMe, *t*-BuOH, 23°C, 12 h; (f) MeOCOCl, *i*Pr_2NEt, NaN_3 then *t*BuOH, 80°C, 12 h (42% from **9**); (g) *n*$Bu_4N^+F^-$, THF, 0°C, 30 min; (h) $RuCl_3$ (cat), $NaIO_4$, MeCN:CCl_4:H_2O, (2:2:3), 23°C, 12 h (66%).

resulting acylazide in the presence of *tert*-butanol furnished the BOC-derivative **10** in 42% overall yield (from **9**). The stereochemistry of the BOC-amine derivative in **10** was assigned based upon the evidence that the Curtius rearrangement proceeds with retention of configuration of the migrating carbon atom.[11] To complete the synthesis of protected 5-*O*-carbamoylpolyoxamic acid **11**, the silyl protecting group was removed by treatment with tetrabutylammonium fluoride in THF and the resulting alcohol was oxidized with a catalytic amount of ruthenium chloride in the presence of sodium periodate to afford **11** in 66% yield after chromatography.[12] The spectral properties (^{1}H NMR and ^{13}C-NMR) of **11** ($[\alpha]_D^{23}$ +0.4, *c* 2.2, acetone; lit.[4j] $[\alpha]_D^{26}$ +0.3, *c* 1.5, acetone) are in full agreement with the literature values.

Conclusion

In conclusion, the [2,3]-Wittig-Still rearrangement of isopropylidene L-threitol derived *E*-, *Z*-stannyl ethers has exhibited noteworthy stereoelectronic effects. The *E*-allylic stannyl ether derivative has shown better *syn*-diastereoselectivity (5.4:1) than the corresponding *Z* isomer (2:1). Presumably, the lack of diastereoselectivity is due to competing electronically favored and sterically favored transition states. The stereochemical assignment of the major diastereomer **6** was made conclusively through its conversion to known 5-*O*-carbamoylpolyoxamic acid derivative **11** which is an amino acid component of many bioactive polyoxins.

Experimental Section

All melting points were recorded on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Proton magnetic resonance spectra were recorded on Bruker AC 200 and AM 400 MHz spectrometers using tetramethylsilane as internal standard. IR spectra were recorded on a ATI Mattson Genesis series FT-IR spectrometer. Mass spectra were recorded on a Finnigan Mat 90 mass spectrometer and relevant data are tabulated as m/z. Optical rotation was measured on a Perkin-Elmer 241 spectropolarimeter. Anhydrous solvents were obtained as follows: tetrahydrofuran, distillation from sodium and benzophenone; methylene chloride, distillation from CaH_2; pyridine, distillation from CaH_2. All other solvents were HPLC grade. Column chromatography was performed with Whatman 240-400 mesh silica gel under low pressure of 5-10 psi. Thin-layer chromatography (TLC) was carried out with E. Merck silica gel 60 F-254 plates.

(*Z*)-(2*S*,3*S*)-1-*O*-Benzyl-2,3-*O*-(1-methylethylidene)-1,2,3,6-tetrahydroxy-hex-4-ene (3). To a stirred solution of DMSO (0.95 mL, 13.4 mmol) in CH_2Cl_2 (10 mL) at -78 °C was added oxalyl chloride (0.7 mL, 8.01 mmol) dropwise. After 2 minutes, alcohol **1** (1.35 g, 5.34 mmol) in CH_2Cl_2 (2 mL) was added dropwise. The mixture was stirred at -78°C for 30 minutes. After this period, Et_3N (3.5 mL, 26.7 mmol) was added dropwise. The resulting mixture was stirred at -78°C for an additional 2 minutes and then allowed to warm to 23°C. The reaction mixture was evaporated under reduced pressure and the residue was dissolved in EtOAc. The resulting mixture was washed with cold aqueous $NaHSO_4$ (1 M), brine, dried (anhydrous Na_2SO_4) and evaporated to give a residue which was used directly without further purification.

To a stirred solution of bis(2,2,2-trifluroethyl)methoxycarbonylmethylphosphonate (1.24 mL, 5.87 mmol) and 18-crown-6 (7.05 g, 26.7 mmol) in dry THF (20 mL) at -78°C was added $KN(TMS)_2$ (12.8 mL, 6.40 mmol) dropwise. The resulting mixture was stirred for 30 min. After this period, the above aldehyde in THF (2 mL) was added dropwise and the resulting mixture was stired for 40 min. After this period, the mixture was quenched with saturated aqueous NH_4Cl solution and warmed to 23°C. The layers were separated and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine and dried over

anhydrous Na_2SO_4. Evaporation of the solvent gave a residue which was chromatographed on silica gel to furnish the mixture (95:5 by 400 MHz ^{1}H-NMR) of *Z*- and *E*-ester (1.17 g, 71%) as a colorless oil. *Z*-isomer: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.30 (m, 5H), 6.21 (dd, *J* = 11.6, 8.5 Hz, 1H), 5.94 (dd, *J* = 11.6, 1.6 Hz, 1H), 5.39 (m, 1H), 4.60 (dd, *J* = 17.2, 12.0 Hz, 2H), 3.60 - 3.75 (m, 2H), 3.67 (s, 3H), 1.46 (s, 6H).

To a stirred solution of the above ester (1.15 g, 3.76 mmol) in CH_2Cl_2 (10 mL) was added Dibal (1.0 M in hexane, 11.5 mL, 11.5 mmol) at -78°C. The resulting mixture was stirred for 2 h at -78°C. After this period, the reaction mixture was carefully quenched with water (3 mL) and was allowed to warm to 23°C. The mixture was filtered through a glass wool plug and the solid was rinsed several times with CH_2Cl_2 and water. The filtrate was transfered to a seperatory funnel and the layers were separated. The aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4 and evaporated to give a residue which was purified on a silica gel column (25% EtOAc/hexane) to afford **3** as a colorless oil (887 mg, 85%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.33 (m, 5H), 5.87 (m, 1H), 5.56 (m, 1H), 4.71 (t, *J* = 8.7 Hz, 1H), 4.58 (dd, *J* = 17.2, 12.0 Hz, 2H), 4.13 (m, 2H), 3.87 (m, 1H), 3.62 (d, *J* = 4.7 Hz, 2H), 2.04 (m, 1H), 1.43 (s, 6H); ^{13}C-NMR(100 MHz, $CDCl_3$) δ 137.4, 133.7, 128.9, 128.4, 127.8, 109.4, 79.6, 74.1, 73.6, 69.3, 58.4, 26.9, 26.8.

(2*S*,3*S*,4*R*)-1-*O*-Benzyl-4-hydroxymethyl-2,3-*O*-(1-methylethylidene)-1,2,3-trihydroxy-hex-5-ene (6). To a stirred suspension of KH (440 mg, 11 mmol, prewashed with hexane) and tetrabutylammonium iodide (20 mg) in dry THF (20 mL) at 0°C was added dropwise a solution of alcohol **2** (1.02 g, 3.67 mmol) in THF (2 mL). The resulting red suspension was allowed to warm to 23°C, and the mixture was stirred for 1 h. The reaction mixture was cooled to 0°C, and Bu_3SnCH_2I (1.89 g, 4.40 mmol) in THF (2 mL) was added dropwise over a period of 2 min. The mixture was stirred at 23°C for 4 h. After this period, the reaction was quenched with a saturated NH_4Cl solution (10 mL). The layers were separated, and the aqueous layer was extracted with EtOAc. The combined organic layer was dried over anhydrous Na_2SO_4. Evaporation of the solvent provided the stannyl ether **4** as a colorless oil which was used for the next reaction without further purification.

To a stirred solution of the above crude stannyl ether **4** in THF (10 mL) at -78°C was added *n*BuLi (3.4 mL, 5.4 mmol; 1.6 M in hexane) dropwise by a syringe pump over a period of 1 h. The resulting mixture was stirred at -78°C for 2 h. After this period, the reaction was quenched with saturated NH_4Cl solution and the resulting mixture was warmed to 23°C. The layers were separated, and the aqueous layer was extracted with EtOAc. The combined layers were dried over anhydrous Na_2SO_4. Evaporation of the solvent gave a residue which was chromatographed over silica gel (25% EtOAc/hexane) to furnish an inseparable mixture (5.4:1 by ^{1}H NMR) of **6** and its epimer **7** (869 mg, 81% from **2**; R_f 0.29, 25% EtOAc/hexane) as a colorless oil. Major isomer **6**: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.34 (m, 5H), 5.85 (m, 1H), 5.25 (dd, *J* = 10.3, 1.7 Hz, 1H), 5.16 (dd, *J* =17.6, 1.7 Hz, 1H), 4.57 (dd, *J* = 14.8, 12.1 Hz, 2H), 4.02 (m, 2H), 3.68 (d, *J* = 6.2 Hz, 2H), 3.57 (m, 2H), 2.39 (m, 1H), 2.28 (brs, 1H), 1.38 (s, 6H); ^{13}C-NMR(50 MHz, $CDCl_3$) δ 137.7, 134.4, 128.3, 127.7, 127.6, 119.3, 109.3, 78.5, 77.1, 73.4, 70.4, 64.2, 47.9, 26.9, 26.8. Anal. Calcd for $C_{17}H_{24}O_4$: C, 69.84; H, 8.27. Found: C, 69.31; H, 8.27. Minor isomer **7**: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.38 - 7.26 (m, 5H), 5.49 (m, 1H), 5.18 (dd, *J* = 10.3, 1.7 Hz, 1H), 5.09 (dd, *J* = 17.6, 1.7 Hz, 1H), 4.57(dd, *J* = 14.8, 12.1 Hz, 2H), 3.75 - 3.90 (m, 2H), 3.45 - 3.70 (m, 4H), 2.39 (m, 1H), 2.28 (brs, 1H), 1.42 (s, 6H).

(2*S*,3*S*,4*S*)-1-*O*-Benzyl-4-hydroxymethyl-2,3-*O*-(1-methylethylidene)-1,2,3-trihydroxy-hex-5-ene (6) (prepared form *Z*-alcohol **3**). The *Z*-alcohol **3** (639 mg, 2.30 mmol) was converted to *Z*-stannyl ether

5 as a colorless oil by following the procedure described for *E*-stannyl ether **4**. The material was used for the next reaction without further purification. Wittig-Still rearrangement of *Z*-stannyl ether **5** as described for **4** provided an inseparable mixture (2:1 by ^{1}H-NMR) of alcohols **6** and **7** (493 mg, 73%) as a colorless oil.

(2*S*,3*S*,4*R*)-1-*O*-Benzyl-4-[(1,1-dimethylethyl)dimethylsilyloxymethyl]-2,3-*O*-(1-methylethyli-dene)-1,2,3-trihydroxy-hex-5-ene (8). The mixture of diastereomers **6** and **7** (620 mg, 2.12 mmol) was dissolved in DMF (6 mL). The mixture was cooled to 0°C. Imidazole (216 mg, 3.18 mmol) was added. After stirring for 5 min, *tert*-butyldimethylsilyl chloride (384 mg, 2.55 mmol) was added portionwise. The resulting mixture was stirred at 23°C for 12 h. After this period, the mixture was diluted with EtOAc, washed with water and brine. Evaporation of the solvent gave a residue which was chromatographed over silica gel (2% EtOAc/hexane) to give **8** as a colorless oil (660 mg, 77%; R_f 0.49, 10% EtOAc/hexane) along with its diastereomer (134 mg, 16%): $[\alpha]_D^{23}$-16.8 (*c* 1.34, $CHCl_3$); Compound **8**: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.34 (m, 5H), 5.80 (m, 1H), 5.19 (dd, *J* = 10.4, 1.9 Hz, 1H), 5.16 (dd, *J* = 17.7, 1.9 Hz, 1H), 4.58 (dd, *J* = 19.0, 12.2 Hz, 2H), 4.04 (m, 2H), 3.68 (dd, *J* = 9.9, 2.1 Hz, 1H), 3.56 - 3.62 (m, 3H), 2.35 (m, 1H), 1.38 (s, 6H), 0.88 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 138.0, 134.5, 128.2, 127.4, 118.8, 108.7, 77.3, 76.4, 73.3, 70.5, 64.0, 48.1, 26.9, 26.9, 25.8, 18.2, -5.4, -5.5.

(2*S*,3*S*,4*R*)-1-*O*-Aminocarbonyl-4-[(1,1-dimethylethyl)dimethylsilyoxymethyl]-2,3-*O*-(1-meth-ylethylidene)-1,2,3-trihydroxy-hex-5-ene (9). To a stirred solution of lithium (13 mg, 1.86 mmol) in liquid ammonia (10 mL) was added a solution of **8** (226 mg, 0.56 mmol) in THF (2 mL) at -30°C. The resulting mixture was stirred for 30 min. Solid NH_4Cl was added until the blue color disappeared. The mixture was allowed to warm to 23°C. Water (10 mL) and EtOAc (10 mL) were added. The layers were separated and the aqueous layer was extracted with EtOAc (2 X 20 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and evaporated. The residue was dissolved in CH_2Cl_2 (3 mL). Pyridine (0.5 mL) followed by *p*-nitrophenylchloroformate (305 mg, 1.51 mmol) were added at 0°C. The resulting mixture was stirred at 0°C for 1 h. After this period, the mixture was diluted with CH_2Cl_2 and washed with saturated aqueous $NaHCO_3$, brine and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave a pale yellow solid which was dissolved in THF (3 mL). The resulting mixture was cooled to 0°C, and aqueous ammonia (0.5 mL) was added. After stirring for 30 min at 0°C, the mixture was diluted with EtOAc, washed with saturated aqueous $NaHCO_3$ and brine, and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave a residue which was chromatographed over silica gel (15% EtOAc/hexane) to give **9** as a white solid (179 mg, 88%; m.p. 88 - 90°C; R_f 0.28, 25% EtOAc/hexane): $[\alpha]_D^{23}$-21 (*c* 0.07, $CHCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.74 (m, 1H), 5.18 (dd, *J* = 10.4, 1.8 Hz, 1H), 5.13 (dd, *J* = 17.5, 1.8 Hz, 1H), 5.10 (brs, 2H), 4.27(m, 1H), 3.98 - 4.02 (m, 3H), 3.63 (m, 2H), 2.32 (dd, *J* = 16.3, 8.3 Hz, 1H), 1.35 (s, 6H), 0.86 (s, 9H), 0.02 (s, 3H), 0.01 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 156.8, 134.2, 118.9, 109.0, 76.4, 76.0, 65.1, 63.8, 48.0, 26.9, 26.8, 25.7, 18.1, -6.0, -6.1. Anal. Calcd for $C_{17}H_{33}NO_5Si$: C, 56.79; H, 9.25; N, 3.90. Found: C, 57.12; H, 9.19; N, 3.68.

(1*R*)-4-*O*-Aminocarbonyl-1-[(1,1-dimethylethyl)dimethylsilyloxymethyl]-1-[((1,1-dimethyleth-yl)oxycarbonyl)amino]-1-deoxy-2,3-*O*-(1-methylethylidene)-L-threitol (10). Through a solution of **9** (128 mg, 0.36 mmol) in a mixture of CH_2Cl_2 (1 mL) and MeOH (1 mL) at -78°C was bubbled through a stream of ozonized oxygen until the blue color persisted. After the solution was flushed with oxygen for 5 min, Me_2S (0.5 mL) was added to the reaction mixture at -78°C. Then the dry ice bath was removed and reaction

mixture was warmed to 23°C. Evaporation of the solvents under reduced pressure gave the crude aldehyde which was dissolved in a mixture of *tert*-butyl alcohol (5 mL) and 2-methyl-2-butene (1 mL). To this stirred mixture at 23°C, a solution of $NaClO_2$ (400 mg, 3.56 mmol; 80% purity) and $NaH_2PO_4 \cdot H_2O$ (492 mg, 3.56 mmol) in water (2 mL) was slowly added. The resulting mixture was stirred at 23°C for 12 h. After this period, the mixture was diluted with saturated aqueous NH_4Cl and was extracted with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4. Evaporation of the solvent provided the acid which was used directly for the next reaction.

To a stirred solution of the above acid in acetone (4 mL) was added diisopropylethyl amine (81 μl, 0.45 mmol) at 0°C. The resulting mixture was stirred for 10 min, and MeOCOCl (33 μl, 0.43 mmol) was added dropwise over a period of 1 min. The reaction mixture was stirred for 30 min at 0°C, then NaN_3 (47 mg, 0.72 mmol) in water (2 mL) was added. The mixture was stirred for an additional 30 min at 0°C. After this period, CH_2Cl_2 and water were added and the layers were separated. The organic layer was washed with cold aqueous $NaHSO_4$ solution (1 M), pH 7 buffer and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave a residue which was dissolved in *tert*-butyl alcohol (2 mL). The resulting mixture was refluxed at 80°C for 12 h. After this period, the mixture was cooled to 23°C, and the solvent was evaporated to give a residue which was purified by silica gel chromatography (25% EtOAc/hexane) to furnish the Boc derivative **10** (66 mg, 42%; R_f 0.19, 25% EtOAc/hexane) as a colorless oil: $[\alpha]_D^{23}$ -18.8 (*c* 3.99, $CHCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.05 (brs, 2H), 4.80 (d, *J* = 9.6 Hz, 1H), 4.17 (m, 2H), 4.12 (m, 1H), 3.99 (m, 1H), 3.78 (m, 1H), 3.65 (m, 1H), 3.54 (t, *J* = 9.0 Hz, 1H), 1.41 (s, 9H), 1.40 (s, 3H), 1.36 (s, 3H), 0.87 (s, 9H), 0.04 (s, 6H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 156.2, 155.6, 109.4, 79.5, 76.2, 75.0, 64.6, 62.7, 50.9, 28.2, 26.8, 26.6, 25.7, 18.1, -5.5.

5-*O*-(Aminocarbonyl)-2-[((1,1-dimethylethyl)oxycarbonyl)amino]-2-deoxy-3,4-*O*-(1-methyleth-ylidene)-L-xylonic acid (11). To a stirred solution of **10** (48 mg, 0.11 mmol) in THF (2 mL) at 0°C was added nBu$_4$N$^+$F$^-$ (0.16 mL, 0.16 mmol; 1 M in THF). The resulting mixture was stirred at 0°C for 30 min. After this period, the mixture was quenched with saturated aqueous NH_4Cl, and the layers were separated. The aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave the crude alcohol which was dissolved in a mixture (2:2:3) of MeCN:CCl_4:H_2O (3.5 mL). To this mixture was added $NaIO_4$ (95 mg, 0.44 mmol) and $RuCl_3$ (2 mg). The resulting suspension was stirred for 12 h at 23°C. After this period, CH_2Cl_2 and water were added. The layers were separated. The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave a residue which was chromatographed over silica gel using a mixture (50:50:1) of Et_2O:EtOAc:HOAc to furnish **11** (25 mg, 66%) as a white foam: $[\alpha]_D^{23}$ +0.4 *c* 2.2, acetone; lit.[4j] $[\alpha]_D^{26}$ +0.3 *c* 1.5, acetone; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.33 (d, *J* = 9.6 Hz, 1H), 5.29 (s, 2H), 4.51 (d, *J* = 9.6 Hz, 1H), 4.36 (d, *J* = 7.4 Hz, 1H), 4.28 (m, 2H), 4.03 (m, 1H), 1.45 (s, 9H), 1.39 (s, 3H), 1.38 (s, 3H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 172.9, 157.0, 156.0, 110.1, 80.6, 78.0, 74.9, 64.0, 52.9, 28.3, 26.8, 26.7; MS (FAB) *m/z* 349 (M^+ + 1), 293, 249, 235. HRMS (FAB) Calcd for $C_{14}H_{25}N_2O_8$ (M^+ + 1): 349.1611. Found: 349.1615.

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