Pergamon

Tetrahedron 54 (1998) 9303–9316

TETRAHEDRON

Stereocontrolled and enantioselective synthesis of the branched 6-amino-4,6-deoxyheptopyranuronic acid component of amipurimycin

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Received 18 February 1998; accepted 9 June 1998

Key Words: amino acids and derivatives; asymmetric synthesis; carbohydrates; stereocontrol.

Abstract

*A stereocontrolled and enantioselective synthesis of the branched 6-amino-4,6-deoxyheptopyranuronic acid component of amipurimycin is reported. Key stages in the synthesis include the stereodivergent assembly of the dihydropyrones **12** and **14** from serinal derivatives (S)-**10** and (R)-**10**, elaboration of the tetrahydropyran ring to give **26** and **31**, and finally, introduction of the cis-2-aminocyclopentanecarboxylic acid moiety to produce the diastereomeric peptides **28/29** and **32/33**.* © 1998 Elsevier Science Ltd. All rights reserved.

INTRODUCTION

Amipurimycin (**1**) [1] and the miharamycins (**2**) [2] are structurally related nucleoside antibiotics, isolated respectively from *Streptomyces novoguineensis* and *S. miharaensis*, which show good activity against rice blast and other fungal diseases. Both of these families of natural products are made up of unusual branched sugar amino acids appended to an N-terminal amino acid residue and a glycosidic purine nucleobase (see Scheme 1). Goto and coworkers proposed structure **1** for amipurimycin based on extensive spectroscopic data in combination with chemical degradation studies [3]. Vigorous acidic hydrolysis of amipurimycin methyl ester produced cis-2-aminocyclopentanecarboxylic acid (**4**). Although the absolute configuration of this compound was not reported, it is of interest to note that (*1R, 2S*)-configured **4** has itself been isolated from *S. setonii* and shown to possess antifungal properties [4]. Exposure of **1** to hot TFA resulted in the isolation of free 2-aminopurine (**5**). UV and NMR data suggested that this nucleobase was incorporated into **1** as its N^9-β-glycoside. The proposed structure of the 3-[1,2-dihydroxyethyl]-6-amino-(4,)6-deoxyheptouronic acid component **6** was based on a series of NMR experiments performed on derivatives of the intact antibiotic. Using a similar approach, Seto and his coworkers proposed structures **2** and **3** for miharamycin A and B respectively. Among the points left

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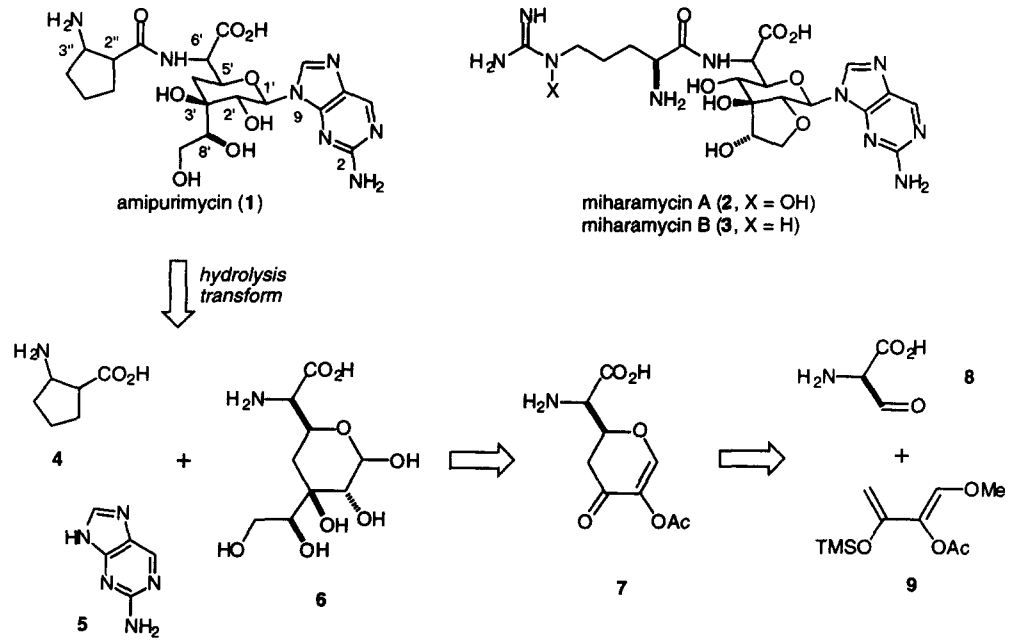
0040-4020/98/$19.00
PII: S0040-4020(98)00585-7

unresolved by these structural studies was the relative stereochemistry at C-6' as well as the absolute configuration of these molecules, making flexibility an important part of any contemplated synthesis plan. To date, no member of these two families of nucleoside antibiotics have yielded to total synthesis. Most of the synthetic work reported so far has focused on elaboration of the branched 6-amino-4,6-deoxyheptopyranuronic acid (sugar) component of these antibiotics. In this context, strategies for attaching the 2-aminopurine nucleobase [5], 1,2-ethanediol branch [6], and glycine moiety [7] to appropriately substituted pyranosides have been worked out. Most recently, Czernecki and coworkers reported the synthesis of a molecule that corresponds to **1** minus the C-3 branch [8]. We now describe a stereocontrolled synthesis of both C-6 diastereomers of **6** as well as the 4 diastereomers corresponding to the intact dipeptidyl glycoside core of **1** [9].

Scheme 1

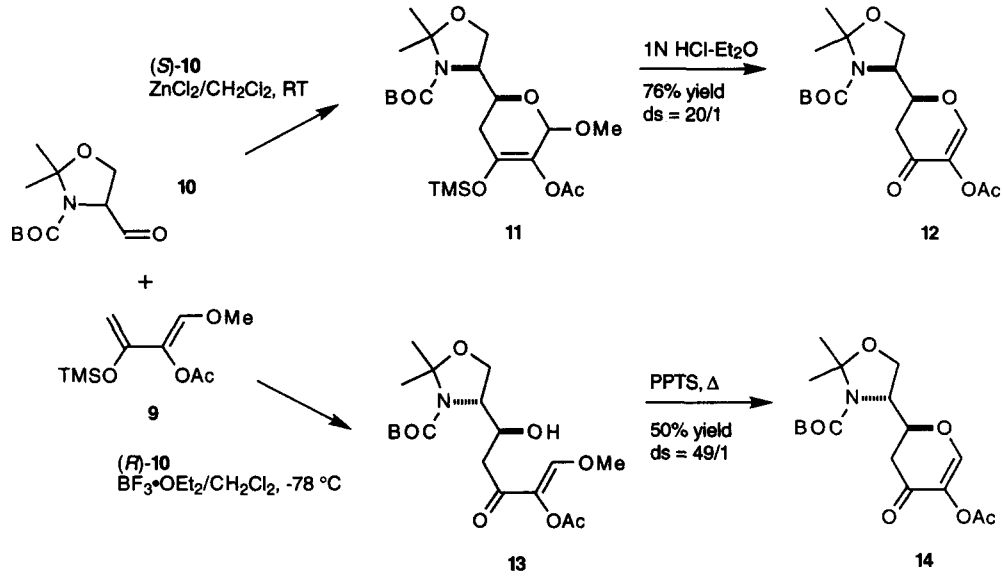


RESULTS AND DISCUSSION

Our retrosynthetic analysis of the problem (Scheme 1) suggested that a suitably protected/masked form of **6** could be coupled with protected versions of **4** and **5** (the order of these events to be determined) to give **1** after final deprotection. Further disconnection led to the dihydropyrone **7**, which would serve as the precursor to **6**. Compound **7** was envisioned to arise from a cyclocondensation of a masked version of penaldic acid **8** and the electron-rich diene **9**. Since the stereochemistry of amipurimycin at C-6' was not determined, we felt that a stereodivergent route to both diastereomers of **7** would be most desirable. Our synthesis begins (Scheme 2) with the oxazolidine aldehyde **10**, a compound that serves as a penaldic acid equivalent [10], and whose (*S*)- and (*R*)-antipodes are readily

prepared from L- and D-serine respectively [11]. We had already shown that (*S*)-**10** reacts with diene **9** [12] in the presence of $ZnCl_2$ to give a good yield of the *syn*- (*threo*-) dihydropyrone **12** via the cycloadduct **11** [13]. However, the complementary aldol-based route to the acetoxy-substituted *anti*- (*erythro*-) dihydropyrone **7b** was at the time wanting due to our inability to form a stable lithium dienolate of 3-acetoxy-4-methoxy-3-buten-2-one. This problem was initially overcome by using Noyori's variation [14] of the Mukaiyama reaction. Thus, **9** itself reacted with (*R*)-**10** in the presence of fluoride to give the dihydropyrone **14** (ds = 14/1, 40% yield) after cyclization of the intermediate aldol **13**. An even better solution was subsequently discovered and involved the BF_3-catalyzed Mukaiyama aldol reaction [15] which raised the yield of **14** to 50% and the ds to 49/1.

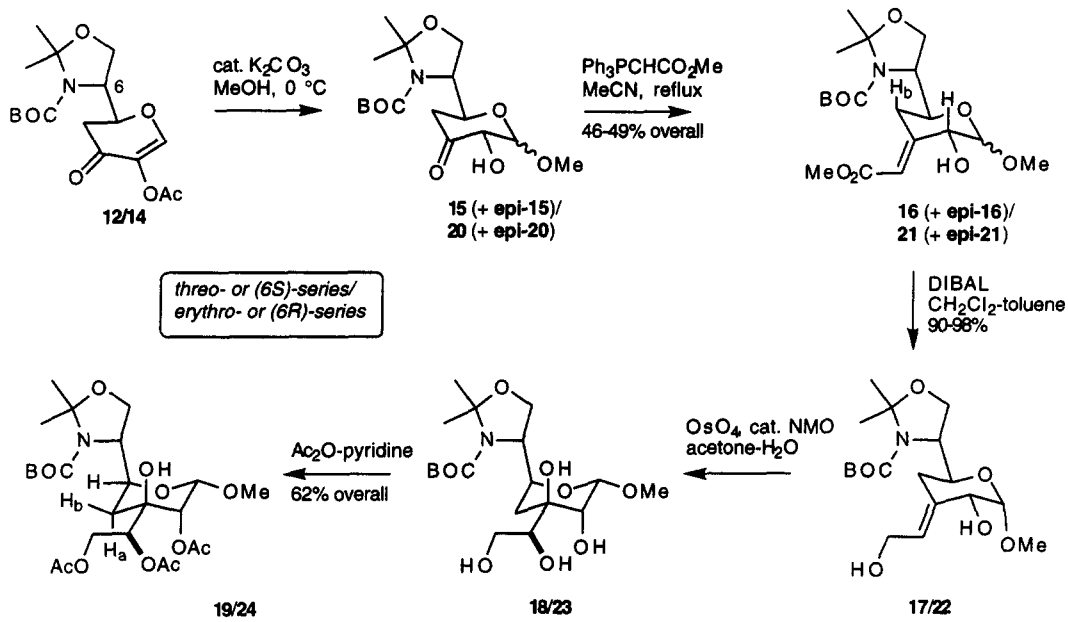
Scheme 2



With **12** and **14** in hand, we set out to elaborate the pyran ring for both the *threo* and *erythro* series as shown in Scheme 3. The sequence commenced with base-catalyzed conjugate addition of methanol to the *threo*-dihydropyranone **12** to give a mixture of sensitive hydroxy ketones **15** [16]. This crude mixture underwent "hydroxyl-directed" Wittig olefination with Ph_3PCHCO_2Me to give the (*E*)-unsaturated esters **16** + **epi-16** (α:β = 5:1) in 46-49% combined yield [17]. The resulting mixture of C-1 diastereomers (reflecting the facial selectivity of conjugate addition step) was separated at this point by means of flash chromatography and the remaining synthetic transformations were carried out with the pure α-anomer **16**. Stereochemical assignments at C-1 and C-2 were based on ^{1}H-NMR data obtained for the acetates derived from **16** and **epi-16**, particularly $J_{1,2}$ = 4.2 Hz for the α- and $J_{1,2}$ = 7.7 Hz for the β-anomer along with NOE difference experiments that showed significant enhancement of the H-2 signal upon H-4b presaturation in both compounds. Reduction of **16** with DIBAL at 0 °C was uneventful and gave the allylic diol **17** in 90-98%

yield. Literature precedent with related 4-alkylidene pyrans suggested that bulky reagents should prefer to approach the exocyclic olefin **17** from its less hindered β-face [18]. In the event, cis-hydroxylation with a catalytic amount of OsO_4 in the presence of stoichiometric N-methylmorpholine-N-oxide produced a single tetraol **18** which was directly acylated with Ac_2O-pyridine to give a triacetate **19** in 62% overall yield after flash chromatography. Application of the same sequence to the *erythro*-dihydropyranone **14** resulted in the production of diastereomeric *erythro*-triacetate **24** in roughly the same overall yield. Interestingly, the ^1H NMR spectrum suggested that the tetrahydropyran ring of **24** had adopted a (distorted) $_4C^1$ conformation ($J_{1,2} = 0$, $J_{4a,5} = 6.6$, & $J_{4b,5} < 1$ Hz) versus the $^4C_1$ conformation of **22** ($J_{1,2} = 4.0$, $J_{4a,5} = 2.3$, & $J_{4b,5} = 12.6$ Hz).

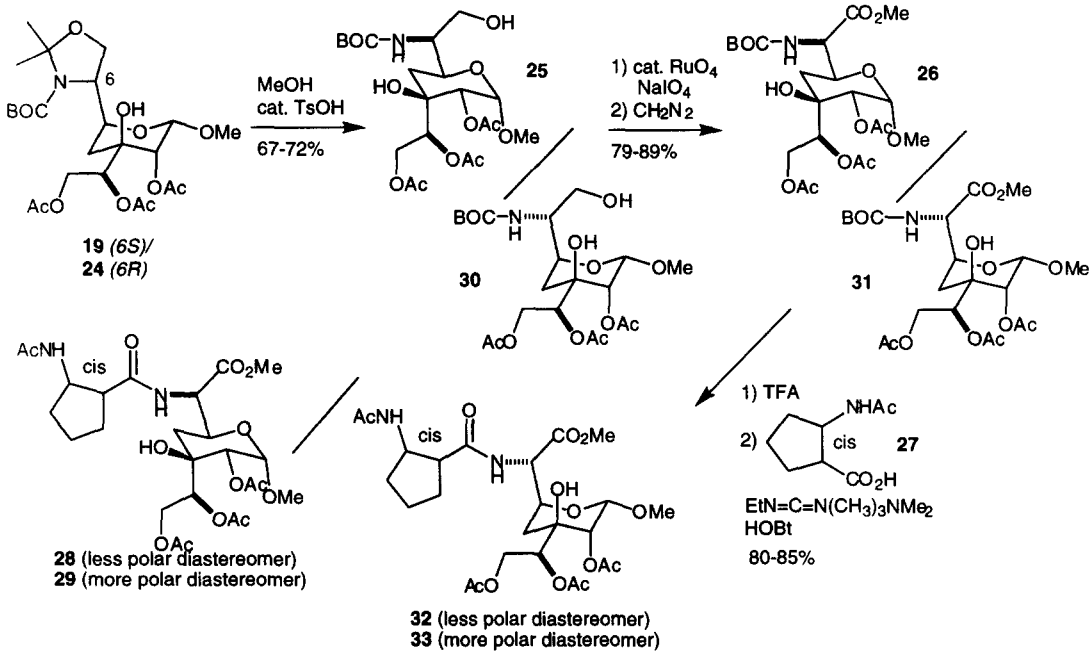
Scheme 3

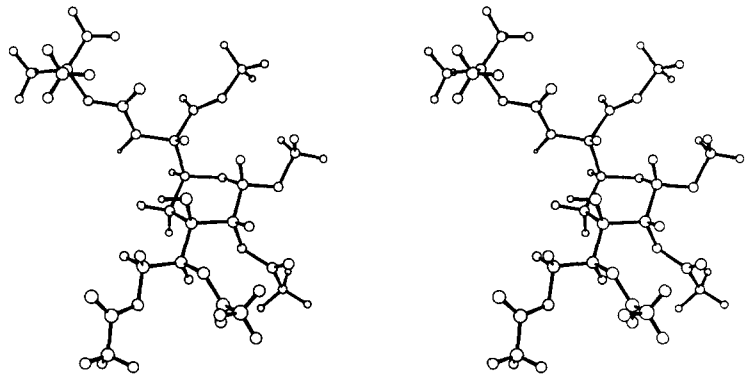


Unmasking of the latent glycyl moiety at C-5 and peptide bond formation began with chemoselective methanolysis of the oxazolidine ring of **19** using TsOH as catalyst to give the diol **25** in 67-72% yield. Oxidation of **25** was readily accomplished with a catalytic amount of $RuO_2 \cdot H_2O$ using $NaIO_4$ as the carrier oxidant and the resulting carboxylic acid was esterified with diazomethane to give the fully protected 6-amino-4,6-deoxyheptopyranuronic acid methyl ester **26** in 79-89% overall yield. At this point, the BOC protecting group was removed with trifluoroacetic acid (TFA) and the resulting free amine was condensed with (±)-2-acetamidocyclopentane-1-carboxylic acid (**27**) [19] to give a 1:1 mixture of diastereomers **28/29** in 80-85% combined yield. An analogous mixture of peptide diastereomers **32/33** was produced when this same sequence was applied to the *erythro*-series via compounds **30** and **31** (which correspond to the C-6 diastereomers of **25** and **26**). The absolute stereochemistry of the individual peptide diastereomers was not determined at

this point, but in both the *threo*- and *erythro*-series they could be separated by flash chromatography and classified as the less polar (**28** and **32**) and more polar (**29** and **33**) diastereomers. It should be noted that alcohol **30** was shown to be configurationally pure (>99% ee) via ^{1}H NMR analysis of the diastereomeric Mosher esters **34** and **35** derived from (*R*)- and (*S*)-methyltrifluorophenylacetic acid (MTPA) respectively. The stereochemistry of **31** was unambiguously determined by X-ray crystallography [20] and showed that this compound was in the $_4C^1$ conformation in the solid state. Although it is difficult to assign solution conformations with certainty, the *threo*-compounds (**25**, **26**, and **28/29**) appear to be in the $^4C_1$ conformation while the *erythro*-series (**30**, **31**, and **32/33**) seem to adopt the $_4C^1$ conformation. This differing conformational behavior is possibly due to intramolecular H-bonding between the urethane/amide NH and O-3 in the *erythro*-series.

Scheme 4





3D structure from x-ray analysis of ***31***

EXPERIMENTAL SECTION

TLC analysis was performed on E. Merck 0.25 mm precoated silica gel 60 F-254 plates and visualized with UV illumination following by charring with either 0.3% ninhydrin in (97:3) n-BuOH-AcOH (char A) or 5% anisaldehyde in (95:5:1) EtOH-AcOH-H_2SO_4 (char B). Melting points are uncorrected. NMR experiments were performed at room temperature unless otherwise indicated. ^1H NMR signal assignments [21] were based on the selective homonuclear decoupling or COSY experiments, while the ^{13}C signal assignments were based on a combination of APT (attached proton test)/HETCOR experiments and proton coupling data. High resolution mass spectra (HRMS) data are reported in units of m/e for M^+ or highest mass fragment derived from M^+ in electron impact (EI) mode. Fast atom bombardment ionization (FAB) was applied using a glycerol matrix. THF, benzene, and toluene were distilled from Na/benzophenone under N_2. $CHCl_3$, CH_2Cl_2, 1,2-dichloroethane, acetonitrile, DMF, hexamethyldisilazane, and Et_3N were distilled from CaH_2. Trimethylsilyl triflate (TMSOTf) and $TiCl_4$ were each distilled under Ar just prior to use.

(2*S,4'*S**)-2-(2,2-Dimethyl-3-tert-butoxycarbonyl-1,3-oxazolidin-4-yl)-5-acetyloxy-2,3-dihydro-4*H*-pyran-4-one (12).** To a suspension of $ZnCl_2$ (16.2 g, 0.119 mol) in CH_2Cl_2 (160 mL) was added a solution of (*S*)-**10** (40 g, 0.17 mol) in CH_2Cl_2 (170 mL). The reaction mixture was stirred at room temperature for 30 min and cooled to 0 °C. A solution of silylated diene **9** (52 g, 0.23 mol) in CH_2Cl_2 (122 mL) was added at 0 °C and the reaction mixture was stirred at room temperature for 4 h. To the reaction was added 1N HCl (260 mL) and Et_2O (260 mL) and the resulting heterogeneous mixture was stirred vigorously at room temperature for 1 h. The reaction mixture was then extracted with Et_2O (1000 mL x 3), washed with saturated $NaHCO_3$ (300 mL x 2), brine (300 mL x 2) dried over $MgSO_4$ then evaporated to give oily residue (66.0 g), which was purified by flash chromatography (SiO_2, 2:1 hexanes-EtOAc) to afford pure pyranone **12** (44.6 g, 72% isolated yield) as a white solid. R_f 0.54 (1:1 hexanes-EtOAc, char A); mp 87-88 °C; $[\alpha]_D^{20}$ +6.5° (*c* 0.89, $CHCl_3$); IR ($CHCl_3$) 1760, 1684, 1626 cm^{-1}; ^1H NMR (300 MHz, C_6D_6, 60 °C) δ 6.90 (s, H-6), 4.71 (m, H-2), 4.06 (m, H-4'), 3.67 (d, J = 8.8 Hz, H-5'$_a$), 3.56 (dd, J = 9.9, 6.3 Hz, H-5'$_b$), 2.63 (dd, J = 17.1, 14.0 Hz, H-5$_a$), 2.52 (dd, J = 17.0, 4.3 Hz, H-5$_b$), 1.86 (s, OAc), 1.55 (s, CH_3), 1.39 (s, CH_3), 1.37 (s, BOC); ^{13}C NMR (75.4 MHz, C_6D_6, 60 °C) δ 184.3, 168.5, 133.4 (3 x CO), 154.7 (C-6), 128.4 (C-5), 95.0 (C-2'), 80.9 ($CO_2\underline{C}(CH_3)_3$), 79.7 (C-2), 64.0 (C-5'), 58.9 (C-4'), 37.5 (C-5), 28.8 ($CO_2C(\underline{C}H_3)_3$), 27.2 ($CO\underline{C}H_3$), 23.9, 20.1 (2 x CH_3); Anal. Calcd for $C_{17}H_{25}NO_7$: C, 57.46; H, 7.10. Found: C, 57.95; H, 7.16.

(2*S,4'*R**)-2-(2,2-Dimethyl-3-tert-butoxycarbonyl-1,3-oxazolidin-4-yl)-5-acetyloxy-2,3-dihydro-4*H*-pyran-4-one (14).** To a cold (-78 °C) solution of (*R*)-**10** (27.2 g, 0.119 mol) and silylated diene **9** (30.0 g, 0.130 mol) in dry CH_2Cl_2 (340 mL) was added $BF_3{\bullet}OEt_2$ (14.8 mL, 0.12 mol). The reaction mixture was stirred at -78 °C for 1 h, at which time, the TLC in 1:1 hexanes-EtOAc showed the formation of the intermediate aldol, R_f 0.22, and the desired pyranone **14**, R_f 0.54, at the expense of the starting material, R_f

0.76. To the reaction mixture was added saturated $NaHCO_3$ (120 mL) and brine (600 mL) then the solution was extracted with CH_2Cl_2 (500 mL x 3). The combined organic layer was washed with brine (200 mL x 3), dried over $MgSO_4$, then evaporated to give amber oil (50.4 g). This amber oil was dissolved in benzene (500 mL) and PPTS (3.3 g, 12 mmol) was added then the solution was refluxed and slowly distilled for 2 h, at which time, the TLC analysis in (1:1) hexanes-EtOAc showed the formation of product, R_f 0.54, at the expense of the intermediate aldol, R_f 0.22. The cooled amber solution was partitioned between saturated $NaHCO_3$ (500 mL) and Et_2O (2000 mL). The organic layer was washed with brine (200 mL), dried over $MgSO_4$, then evaporated to give crude product (34.6 g) as an amber oil. Flash chromatography (SiO_2, 2:1 hexanes-EtOAc) afforded pure pyranone **14** (21.8 g, 52% yield) as a slightly yellow oil. This compound was found to be 98:2 mixture of *erythro* and *threo* diastereomers by HPLC (analytical SiO_2 column, 3:1 hexanes-EtOAc, 1 mL/min, *Rt threo* 25.5 min, *erythro* 27.3 min). $[\alpha]_D^{23}$ +128° (*c* 2.60, $CHCl_3$); IR ($CHCl_3$) 1770, 1685, 1625, 1370, 1170 cm^{-1}; ^1H NMR (300 MHz, C_6D_6, 60 °C) δ 6.81 (s, H-6), 4.40 (m, H-2), 3.84 (m, H-4'), 3.76 (dd, J = 9.3, 1.5 Hz, H-5'$_a$), 3.46 (dd, J = 9.3, 5.7 Hz, H-5'$_b$), 2.56 (dd, J = 16.9, 13.7 Hz, H-5$_a$), 2.41 (dd, J = 17.0, 4.1 Hz, H-5$_b$), 1.80 (s, OAc), 1.50 (s, CH_3), 1.43 (s, CH_3), 1.32 (s, BOC); ^{13}C NMR (75.4 MHz, C_6D_6, 60 °C) δ 184.0, 168.5, 133.5 (3 x CO), 154.6 (C-6), 129.5 (C-5), 95.1 (C-2'), 81.1 ($CO_2\underline{C}(CH_3)_3$), 80.2 (C-2), 64.6 (C-5'), 59.8 (C-4'), 39.6 (C-5), 28.8 ($CO_2C(\underline{C}H_3)_3$), 27.8 ($CO\underline{C}H_3$), 24.4, 20.1 (2 x CH_3); HRMS calcd for $C_{17}H_{25}NO_7$ (M^+) 355.1631, found 355.1615.

Methyl (4'*R)-5-(2,2-Dimethyl-3-tert-butoxycarbonyl-1,3-oxazolidin-4-yl)-3(*E*)-methoxy-carbonylidene-3,4,6-trideoxy-α-D-glucopyranoside (21).** To a cold (0 °C) solution of **14** (20.0 g, 56.3 mmol) in MeOH (225 mL, 0.25 M) was added K_2CO_3 (1.56 g, 11.3 mmol) and the reaction mixture was stirred at 0 °C for 2 h, at which time, the TLC in 1:1 hexanes-EtOAc showed the formation of α-hydroxy pyranones, R_f 0.56 (β-anomer, minor) and R_f 0.37 (α-anomer, major), at the expense of starting material, R_f 0.54. The reaction mixture was diluted with ether (1000 mL) and washed with brine (100 mL x 2), dried over $MgSO_4$ then evaporated to give an anomeric mixture of α-hydroxy pyranones **20** +**epi-20** (17.7 g, 91% yield) as a yellow foam. This material was dissolved in CH_3CN (205 mL, 0.25 M) and methyl (triphenylphosphoranylidene) acetate (34.27 g, 102.5 mmol, 2 equiv) was added. The reaction mixture was refluxed for 3 h, at which time, the TLC in 1:1 hexanes-EtOAc (char A) showed the formation of Wittig products, R_f 0.53 (β-anomer, minor), R_f 0.49 (α-anomer, major). The reaction mixture was cooled to room temperature, diluted with ether (1000 mL), washed with 1 N HCl (200 mL x 2), brine (200 mL), dried over $MgSO_4$ then evaporated to give deep red oily residue (33.6 g). This crude mixture was recrystallized from hot EtOAc to recover most of the triphenylphosphine oxide. The mother liquor was then purified by flash chromatography (SiO_2, 2:1 hexanes-EtOAc) to give the β-anomer **epi-21** (1.73 g, 7.7% yield) and the α-anomer **21** (8.66 g, 38.3% yield) as solids. For **21**: mp 138-139 °C; $[\alpha]_D^{22}$ +72.4° (*c* 2.17, $CHCl_3$); IR ($CHCl_3$) 1715, 1695, 1390, 1365 cm^{-1}; ^1H NMR (300 MHz, C_6D_6, 60 °C) δ 6.29 (s, H-1"), 4.57 (d, J = 4.2 Hz, H-1), 4.29 (bd, J = 13.7 Hz, H-5), 4.05-3.81 (m, H-4', H-2, H-5'$_a$), 3.63 (dd, J = 8.8, 5.6 Hz, H-5'$_b$), 3.39 (s,

OCH_3), 3.01 (s, CO_2CH_3), 1.95 (br s, OH), 1.91 (bd, J = 10.6 Hz, H-4_a), 1.68 (s, CH_3), 1.53 (s, CH_3), 1.46 (s, BOC); ^{13}C NMR (75.4 MHz, C_6D_6, 60 °C) δ 167.1, 156.8 (2 x CO), 152.9 (C-3), 113.7 (C-1"), 101.7 (C-1), 94.8 (C-2'), 80.4 ($CO_2\underline{C}(CH_3)_3$), 72.2 (C-5), 70.9 (C-2), 65.22 (C-5'), 61.06 (C-4'), 55.32 (OCH_3), 50.96 ($CO_2\underline{C}H_3$), 32.62 (C-4), 28.98 ($CO_2C(\underline{C}H_3)_3$), 27.9, 24.9 (2 x CH_3); HRMS calcd for $C_{18}H_{28}NO_8$ ([M-CH_3]+) 386.1815, found 386.1825.

Methyl (4'*S)-5-(2,2-Dimethyl-3-tert-butoxycarbonyl-1,3-oxazolidin-4-yl)-3(*E*)-methoxy-carbonylidene-3,4,6-trideoxy-α-D-glucopyranoside (16).** 49% isolated yield; R_f 0.40 (1:1 hexanes-EtOAc, char A); mp 49-51 °C; $[\alpha]_D^{25}$ +7.4° (*c* 6.0, $CHCl_3$); IR ($CHCl_3$) 3520, 2950, 1695 cm^{-1}; ^1H NMR (300 MHz, C_6D_6, 60 °C) δ 6.29 (s, H-1"), 4.57 (d, J = 4.0 Hz, H-1), 4.33 (bd, J = 13.7 Hz, H-5), 4.25-4.10 (m, H-2), 4.02 (br d, J = 9.5 Hz, H-$5'_a$), 3.93 (dm, J = 10 Hz, H-4'), 3.72 (dd, J = 9.5, 6.5 Hz, H-$5'_b$), 3.37 (s, OCH_3), 3.07 (s, CO_2CH_3), 1.85 (br s, OH), 1.44 (s, CH_3), 1.39 (s, CH_3, BOC); ^{13}C NMR (75.4 MHz, C_6D_6, 60 °C) δ 166.2, 156.05 (2 x CO), 151.9 (C-3), 113.1 (C-1"), 100.8 (C-1), 94.1 (C-2'), 79.4 ($CO_2\underline{C}(CH_3)_3$), 71.4 (C-5), 68.7 (C-2), 63.3 (C-5'), 59.0 (C-4'), 54.4 (OCH_3), 50.1 ($CO_2\underline{C}H_3$), 28.8 (C-4), 28.0 ($CO_2C(\underline{C}H_3)_3$), 23.7, 22.7 (2 x CH_3); HRMS calcd for $C_{19}H_{31}NO_8$ (M^+) 401.2050, found 401.2034.

Methyl (4'*R)-5-(2,2-Dimethyl-3-tert-butoxycarbonyl-1,3-oxazolidin-4-yl)-3(*E*)-(2-hydroxy-ethan-1-ylidene)-3,4,6-trideoxy-α-D-glucopyranoside (22).** To a cold (-10 °C) solution of **21** (8.02 g, 20.0 mmol) in CH_2Cl_2 (200 mL, 0.1 M) was added DIBAL solution in toluene (40 mL, 1.5 M solution, 59.94 mmol) over a period of 30 min. The reaction mixture was stirred at 0 °C for 30 min, by which time, the TLC analysis in EtOAc showed the formation of allylic alcohol, R_f 0.33, at the expense of starting material. The reaction was quenched by slow addition of methanol (45 mL) in 1 N HCl (85 mL) at 0 °C and allowed to warm to room temperature. The reaction mixture was extracted with EtOAc (500 mL x 3), washed with brine (100 mL), dried over $MgSO_4$ then evaporated to give crude product (7.2 g) as a white foam. Purification by flash chromatography (SiO_2, EtOAc) gave pure allylic alcohol **22** (6.7 g, 90% yield). $[\alpha]_D^{23}$ +90.5° (*c* 2.71, $CHCl_3$); IR ($CHCl_3$) 3420, 1685, 1385, 1260, 1070, 1040 cm^{-1}; ^1H NMR (300 MHz, C_6D_6, 60 °C) δ 5.93 (m, H-1"), 4.61 (d, J = 4.0 Hz, H-1), 4.09-3.88 (m, H-$2"_a$, $2"_b$, 2, 5, 4'), 4.02 (dd, J = 8.8, 1.6 Hz, H-$5'_a$), 3.65 (dd, J = 8.7, 5.8 Hz, H-$5'_b$), 3.10 (s, OCH_3), 2.69 (dd, J = 14.0, 2.3 Hz, H-4_a), 2.06 (br s, OH), 1.85 (bt, J = 12.6 Hz, H-4_b), 1.65 (s, CH_3), 1.53 (s, CH_3), 1.41 (s, BOC); ^{13}C NMR (75.4 MHz, C_6D_6, 60 °C) δ 153.1 (CO), 137.6 (C-3), 122.7 (C-1"), 101.6 (C-1), 94.8 (C-2'), 80.3 ($CO_2\underline{C}(CH_3)_3$), 71.8 (C-5), 70.2 (C-2), 65.0 (C-5'), 61.1 (C-4'), 58.8 (C-2"), 55.4 (OCH_3), 31.8 (C-4), 28.9 ($CO_2C(\underline{C}H_3)_3$), 27.8, 27.4 (2 x CH_3); HRMS calcd for $C_{17}H_{28}NO_7$ ([M-CH_3]+) 358.1866, found 358.1869.

Methyl (4'*S)-5-(2,2-Dimethyl-3-tert-butoxycarbonyl-1,3-oxazolidin-4-yl)-3(*E*)-(2-hydroxy-ethan-1-ylidene)-3,4,6-trideoxy-α-D-glucopyranoside (17).** 98% isolated yield; R_f 0.40 (EtOAc, char A); $[\alpha]_D^{20}$ +58° (*c* 0.68, $CHCl_3$); IR ($CHCl_3$) 3450,

1690, 1380 cm^{-1}; ^1H NMR (300 MHz, C_6D_6, 60 °C) δ 6.03 (m, H-1"), 4.69 (d, J = 3.9 Hz, H-1), 4.18-4.09 (m, H-2"$_a$, 2"$_b$, 2, 5, 4', 5'$_a$), 3.78 (dd, J = 9.3, 6.6 Hz, H-5'$_b$), 3.22 (s, OCH_3), 2.79 (d, J = 14.0 Hz, H-4$_a$), 2.39 (br s, OH), 1.99 (bt, J = 13.1 Hz, H-4$_b$), 1.77 (s, CH_3), 1.50 (s, CH_3), 1.45 (s, BOC); ^{13}C NMR (75.4 MHz, C_6D_6, 60 °C) δ 152.1 (CO), 136.3 (C-3), 122.0 (C-1"), 100.8 (C-1), 94.1 (C-2'), 79.5 ($CO_2\underline{C}(CH_3)_3$), 71.0 (C-5), 68.3 (C-2), 63.4 (C-5'), 59.0 (C-4'), 58.0 (C-2"), 54.5 (OCH_3), 28.0 ($CO_2C(\underline{C}H_3)_3$), 26.4 (2 x CH_3), 27.8 (C-4); HRMS calcd for $C_{18}H_{31}NO_7$ (M^+) 373.2101, found 373.2109.

Methyl (4'*R)-5-(2,2-Dimethyl-3-tert-butoxycarbonyl-1,3-oxazolidin-4-yl)-4,6-dideoxy-3-*C*-((1'*S**)-1,2-diacetyloxyethyl)-α-D-glucopyranoside, 2-Acetate (24).** To a solution of **22** (6.02 g, 16.1 mmol) in acetone (81 mL, 0.5 M) was added a stock solution of OsO_4 (126 mL, prepared by dissolving OsO_4 (0.25 g) and NMO (19.43 g) in 137 mL of H_2O). The reaction mixture was stirred at room temperature for 3 h, at which time, the TLC analysis in EtOAc showed the clean formation of tetraol **23**. The reaction mixture was diluted with EtOAc (1000 mL), washed with 10% sodium bisulfite (100 mL x 2), 1 N HCl (50 mL x 2), saturated $NaHCO_3$ (50 mL x 2), brine (100 mL), dried over $MgSO_4$ then evaporated to give tetraol (5.52 g, 84% yield) as a white foam. This crude tetraol was dissolved in pyridine (40 mL) and Ac_2O (40 mL) was added. The reaction was stirred at room temperature overnight and quenched by slow addition of MeOH (40 mL). The mixture was diluted with CH_2Cl_2 (1000 mL), washed with 1 N HCl (100mL x 2), saturated $NaHCO_3$ (100 mL x 2), brine (100 mL), dried over $MgSO_4$ then evaporated to give crude triacetate (6.25 g). Purification by flash chromatography (SiO_2, 2:1 hexanes - EtOAc) gave pure triacetate **24** (5.3 g, 62% yield over 2 steps). R_f 0.39 (1:1 hexanes-EtOAc, char A); $[\alpha]_D^{23}$ +1.1° (*c* 5.7, $CHCl_3$); IR ($CHCl_3$) 3250, 1740, 1655, 1400, 1370, 1240 cm^{-1}; ^1H NMR (300 MHz, C_6D_6, 60 °C) δ 6.10 (br s, OH), 5.49 (br s, H-2), 5.43 (bd, J = 7.0 Hz, H-1"), 4.91 (s, H-1), 4.77 (dd, J = 11.9, 2.8 Hz, H-2"$_a$), 4.32 (dd, J = 11.8, 8.5 Hz, H-2"$_b$), 4.29 (m, H-4'), 4.10 (d, J = 9.0 Hz, H-5'$_a$), 3.93 (m, H-5), 3.42 (dd, J = 8.5, 5.2 Hz, H-5'$_b$), 3.20 (s, OCH_3), 2.11 (dd, J = 14.8, 6.6 Hz, H-4$_a$), 1.96, 1.90, 1.72 (s, 3 x OAc), 1.82 (bd, J = 14.8 Hz, H-4$_b$), 1.43 (s, CH_3), 1.34 (s, CH_3), 1.32 (s, BOC); ^{13}C NMR (75.4 MHz, C_6D_6, 60 °C) δ 170.9, 170.72, 169.9, 154.8 (4 x CO), 96.1 (C-1), 95.0 (C-3), 82.4 ($\underline{C}(CH_3)_2$), 73.9 ($CO_2\underline{C}(CH_3)_3$), 73.8 (C-5), 71.9 (C-1"), 68.4 (C-2), 65.5 (C-5'), 63.8 (C-2"), 58.6 (C-4'), 56.6 (OCH_3), 28.8 ($CO_2C(\underline{C}H_3)_3$), 28.4 (C-4), 24.8 (2 x CH_3), 21.4, 21.2, 20.9 (3 x $CO\underline{C}H_3$); HRMS calcd for $C_{23}H_{36}NO_{12}$ ([M-CH_3]$^+$) 518.2237, found 518.2244.

Methyl (4'*S)-5-(2,2-Dimethyl-3-tert-butoxycarbonyl-1,3-oxazolidin-4-yl)-4,6-dideoxy-3-*C*-((1'*S**)-1,2-diacetyloxyethyl)-α-D-glucopyranoside, 2-Acetate (19).** 62% isolated yield; R_f 0.39 (1:1 hexanes-EtOAc, char A); $[\alpha]_D^{20}$ +21° (*c* 0.63, $CHCl_3$); IR ($CHCl_3$) 2990, 1750, 1695, 1400, 1370, 1240 cm^{-1}; ^1H NMR (300 MHz, C_6D_6, 60 °C) δ 5.66 (dd, J = 8.0, 3.0 Hz, H-1"), 5.26 (d, J = 4.3 Hz, H-2), 4.91 (br s, H-1), 4.62 (dd, J = 12.0, 3.1 Hz, H-2"$_a$), 4.47 (m, H-5), 4.28 (dd, J = 11.8, 8.0 Hz, H-2"$_b$), 3.95 (m, H-4', H-5'$_a$), 3.70 (dd, J = 9.5, 6.4 Hz, H-5'$_b$), 3.22 (s, OCH_3), 2.10 (dd, J = 14.3, 4.4 Hz, H-4$_a$), 1.90, 1.82, 1.74 (s + m, 3 x OAc + H-4$_b$), 1.68 (s, CH_3), 1.42 (s, CH_3, BOC); ^{13}C NMR (75.4

MHz, C_6D_6, 60 °C) δ 170.8, 170.4, 170.1, 153.1 (4 x CO), 97.8 (C-1), 94.9 (C-3), 80.5 ($\underline{C}(CH_3)_2$), 74.1 (C-5), 73.4 ($CO_2\underline{C}(CH_3)_3$), 72.2 (C-2), 67.2 (C-1"), 64.4 (C-5'), 63.5 (C-2"), 60.0 (C-4'), 55.7 (OCH_3), 34.5 (C-4), 28.9 ($CO_2C(\underline{C}H_3)_3$), 27.5, 27.2 (2 x CH_3), 21.2, 21.1, 20.8 (3 x $CO\underline{C}H_3$); HRMS calcd for $C_{23}H_{36}NO_{12}$ (M^+) 533.2472, found 533.2491.

Methyl (6*R)-6-(tert-Butoxycarbonylamino)-6-(hydroxy-methyl)-4,6-dideoxy-3-*C*-((1'*S**)-1,2-diacetyloxyethyl)-α-D-gluco-pyranoside, 2-Acetate (30).** To a solution of **24** (4.8 g, 9.0 mmol) in MeOH (45 mL, 0.5 M) was added $TsOH•H_2O$ (10 mol%) and the reaction mixture was stirred at room temperature for 2 h, at which time, the TLC in (2:1) EtOAc-hexanes showed the formation of primary alcohol, R_f 0.23, with a trace of starting material. All the solvent was evaporated and the residual foam was purified by flash chromatography (SiO_2, 4:1 EtOAc-hexanes) to give pure **30** (2.9 g, 67% yield) as a foam. R_f 0.23 (2:1 EtOAc-hexanes, char A); mp 62-65 °C; $[\alpha]_D^{23}$ +9.0° (*c* 3.4, $CHCl_3$); IR ($CHCl_3$) 3280, 1745, 1680, 1510, 1370 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.00 (s, H-2), 5.45 (d, J = 8.6 Hz, NH), 5.09-5.06 (m, H-5, H-1'), 4.94 (s, H-1), 4.46 (dd, J = 11.9, 3.1 Hz, H-2'$_a$), 4.20 (m, H-6), 4.08-4.02 (m, H-2'$_b$, H-7$_a$, OH), 3.76 (m, H-7$_b$), 3.47 (s, OCH_3), 2.55 (m, OH), 2.13 (m, H-4$_b$), 2.09, 2.06, 2.02 (s, 3 x OAc), 1.80 (bd, J = 15.1 Hz, H-4$_a$), 1.46 (s, BOC); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 170.9, 170.77, 170.1, 157.4 (4 x CO), 94.9 (C-1), 81.3 (C-3), 72.7 ($CO_2\underline{C}(CH_3)_3$), 72.2 (C-1'), 70.0 (C-2), 66.7 (C-5), 62.4 (C-2'), 60.7 (C-7), 56.8 (OCH_3), 51.2 (C-6), 28.2 ($CO_2C(\underline{C}H_3)_3$), 27.5 (C-4), 20.9, 20.8 (3 x $CO\underline{C}H_3$); HRMS calcd for $C_{21}H_{35}NO_{12}$ (M^+) 493.2159, found 493.2146.

Methyl (6*S)-6-(tert-Butoxycarbonylamino)-6-(hydroxy-methyl)-4,6-dideoxy-3-*C*-((1'*S**)-1,2-diacetyloxyethyl)-α-D-gluco-pyranoside, 2-Acetate (25).** 72% isolated yield; R_f 0.23 (2:1 EtOAc-hexanes, char A); mp 107-109 °C; $[\alpha]_D^{26}$ +20.8° (*c* 1.84, $CHCl_3$); IR ($CHCl_3$) 3450, 3000, 1750, 1710, 1500 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.53 (dd, J = 7.6, 2.9 Hz, H-1"), 5.13 (d, J = 8.9 Hz, NH), 5.03 (d, J = 3.9 Hz, H-2), 4.91 (d, J = 3.7 Hz, H-1), 4.47 (dd, J = 12.0, 2.9 Hz, H-2"$_a$), 4.20-4.10 (m, H-5, H-2"$_b$), 3.84-3.69)m, H-6, H-1'$_a$, H-1'$_b$), 3.38 (s, OCH_3), 2.98 (br s, OH), 2.09, 2.08. 2.04 (s, 3 x OAc), 2.08-2.04 (m, H-4$_a$, H-4$_b$), 1.45 (s, BOC); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 170.9, 170.3, 169.64, 156.4 (4 x CO), 96.5 (C-1), 79.9 (C-3), 72.4 (C-1"), 72.4 ($CO_2\underline{C}(CH_3)_3$), 71.3 (C-2), 67.3 (C-5), 63.2 (C-2"), 62.5 (C-1'), 55.8 (OCH_3), 53.9 (C-6), 34.3 (C-4), 28.3 ($CO_2C(\underline{C}H_3)_3$), 20.9, 20.7 (3 x $CO\underline{C}H_3$); HRMS calcd for $C_{21}H_{35}NO_{12}$ (M^+) 493.2159, found 493.2165.

Methyl [(6*S)-6-(tert-Butoxycarbonylamino)-4,6-dideoxy-3-*C*-((1'*S**)-1,2-diacetyloxy-ethyl)]-α-D-xylo-heptopyranuronate, 1-Methyl-2-acetate (31).** To a solution of **30** (2.5 g, 5.01 mmol) in acetone (254 mL, 0.02 M) was added an aqueous solution of $NaIO_4$ (6.5 g, 30 mmol) in H_2O (90 mL, 0.33 M) and $RuO_2•H_2O$ (0.22 g, 1.7 mmol). The reaction mixture was stirred at room temperature for 3 h then quenched with i-PrOH (50 mL). The reaction mixture was filtered through Celite and the filtrate was evaporated to give crude acid. This crude product was dissolved in Et_2O (51 mL, 0.1 M) and CH_2N_2 solution in ether (~0.2 M) [22] was added at 0 °C. After 30 min, the excess CH_2N_2

was destroyed with AcOH and the reaction mixture was diluted with Et_2O (500 mL), washed with saturated $NaHCO_3$ (50 mL x 2), brine (100 mL), dried over $MgSO_4$ then evaporated to give crude methyl ester as a pale yellow solid. It was purified by flash chromatography (SiO_2, 1:1 EtOAc-hexanes to 2:1 EtOAc-hexanes) to give pure **31** (2.09 g, 79%) as a solid. R_f 0.44 (Et_2O, char A); mp 136-137 °C; $[\alpha]_D^{21}$ +14.7° (*c* 1.02, $CHCl_3$); IR ($CHCl_3$) 1745, 1680, 1510, 1220 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.54 (s, OH), 5.43 (d, J = 8.4 Hz, NH), 5.15 (s, H-2), 5.12 (s, H-1), 5.06 (dd, J = 8.0, 2.9 Hz, H-1'), 4.96 (t, J = 10.6 Hz, H-6), 4.45 (dd, J = 11.9, 3.1 Hz, H-2'$_a$), 4.04 (dd, J = 11.8, 8.0 Hz, H-2'$_b$), 4.07 (m, H-5), 3.80 (CO_2CH_3), 3.45 (OCH_3), 2.09, 2.05, 2.03 (s, 3 x OAc), 2.14-2.09 (m, H-4$_a$, H-4$_b$), 1.45 (s, BOC); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 171.1, 170.7, 170.7, 169.9, 156.3 (5 x CO), 94.9 (C-1), 82.0 (C-3), 73.4 (C-1'), 72.8 ($CO_2\underline{C}(CH_3)_3$), 72.0 (C-2), 66.7 (C-5), 62.3 (C-2'), 56.9 (C-6), 54.2 (OCH_3), 52.6 ($CO_2\underline{C}H_3$), 28.1 ($CO_2C(\underline{C}H_3)_3$), 27.5 (C-4), 20.9, 20.8 (3 x $CO\underline{C}H_3$); HRMS calcd for $C_{22}H_{35}NO_{13}$ (M^+) 521.2108, found 521.2102.

Methyl [(6*S)-6-(tert-Butoxycarbonylamino)-4,6-dideoxy-3-*C*-((1'*S**)-1,2-diacetyloxy-ethyl)]-α-D-xylo-heptopyranuronate, 1-Methyl-2-acetate (26).** 89% isolated yield; R_f 0.38 (Et_2O, char A); $[\alpha]_D^{20}$ +14.2° (*c* 0.49, $CHCl_3$); IR ($CHCl_3$) 3450, 1750, 1720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.55 (bt, J = 5.4 Hz, H-1'), 5.21 (d, J = 9.6 Hz, NH), 4.88 (d, J = 4.0 Hz, H-2), 4.76 (d, J = 4.1 Hz, H-1), 4.40-4.30 (m, H-5, H-6, H-2'$_a$), 4.04 (dd, J = 12.0, 7.1 Hz, H-2'$_b$), 3.69 (s, CO_2CH_3), 3.19 (s, OCH_3), 2.98 (br s, OH), 2.01, 2.00, 1.97 (3 x $COCH_3$, H-4$_a$), 1.81 (dd, J = 13.9, 10.9 Hz, H-4$_b$), 1.38 (s, BOC); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 170.7, 170.5, 170.3, 169.3, 156.0 (CO), 96.8 (C-1), 80.3 (C-3), 72.3 (C-1', $CO_2\underline{C}(CH_3)_3$), 72.2 (C-2), 67.3 (C-5), 62.3 (C-2'), 56.0 (C-6), 55.4 (OCH_3), 52.5 ($CO_2\underline{C}H_3$), 34.6 (C-4), 28.2 ($CO_2C(\underline{C}H_3)_3$), 20.9, 20.8, 20.7 (3 x $CO\underline{C}H_3$); HRMS calcd for $C_{22}H_{35}NO_{13}$ (M^+) 521.2108, found 521.2102.

Methyl [(6*S)-6-[[((1'*R**,2'*S**) or (1'*S**,2'*R**)-2-Acetylaminocyclopentyl)-carbonyl]amino]-4,6-dideoxy-3-*C*-((1'*S**)-1,2-diacetyloxyethyl)]-α-D-xylo-heptopyranuronate, 1-Methyl-2-acetate (32), (33).** To a solution of **31** (1.82 g, 3.49 mmol) in CH_2Cl_2 (34.9 mL, 0.1 M) was added TFA (6.72 mL, 87.3 mmol) and the reaction mixture was stirred at room temperature for 3 h. All the volatiles were evaporated and the residue was dissolved in CH_2Cl_2 (100 mL) and washed with saturated $NaHCO_3$ (20 mL). The aqueous layer (pH ~8) was extracted with CH_2Cl_2 (50 mL x 2) and the combined organic layers were dried over $MgSO_4$, filtered, then evaporated to give free amine (1.32 g, 90% crude yield). To a solution of 2-(N-acetylamino)cyclopentane carboxylic acid (0.91 g, 5.33 mmol)[21] in CH_2Cl_2 (53 mL, 0.1 M) was added 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (**27•HCl**, 1.80 g, 9.40 mmol) and HOBt (0.76 g, 5.6 mmol). The reaction mixture was stirred at room temperature for 30 min then a solution of free amine in CH_2Cl_2 (31 mL, 0.1 M) was added. The reaction was stirred at room temperature for 3 h, at which time TLC analysis in 20:1:1 EtOAc-acetone-MeOH showed the formation of peptides **32** and **33** at R_f 0.49 and 0.39 respectively. The reaction mixture was diluted with CH_2Cl_2 (200 mL), washed with 1 N HCl (50 mL x 2), saturated $NaHCO_3$ (50 mL

x 2), brine (100 mL), dried over $MgSO_4$ then evaporated to give crude product as a foam. The two diastereomeric peptides were separated by flash chromatography (SiO_2, 20:1:0.5 EtOAc-acetone-MeOH) to give the pure peptides (**32**: 0.98 g, **33**: 1.03 g, 80% over 2 steps). **32**: R_f 0.49 (20:1:1 EtOAc-acetone-hexanes, char A); mp 71-73 °C; $[\alpha]_D^{22}$ -59.5° (*c* 1.21, $CHCl_3$); IR ($CHCl_3$) 1740, 1660, 1520, 1235 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.78 (d, J = 5.0 Hz, NHAc), 6.65 (d, J = 8.4 Hz, 6-NH), 6.16 (s, H-2), 5.16 (dd, J = 10.8, 8.4 Hz, H-6), 5.14 (s, H-1), 4.91 (dd, J = 7.7, 1.1 Hz, H-1"), 4.76 (dd, J = 12.5, 1.1 Hz, H-2"$_a$), 4.15 (m, H-2'), 3.99 (dd, J = 12.5, 7.5 Hz, H-2"$_b$), 3.97 (m, H-5), 3.79 (s, CO_2CH_3), 3.44 (s, OCH_3), 3.25 (m, H-1'), 2.11, 2.10, 2.04, 1.98 (s, 4 x $COCH_3$), 2.03-1.56 (m, H-4, H-3', H-4', H-5'); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 175.9, 175.9, 172.3, 171.5, 170.8, 169.8 (6 x CO), 95.0 (C-1), 73.8 (C-1"), 73.1 (C-3), 73.0 (C-2), 66.5 (C-5), 64.0 (C-2"), 56.9, 55.2, 54.2 ($CO_2\underline{C}H_3$, C-1', C-2'), 52.7 (OCH_3), 47.5 (C-6), 30.9, 27.8, 27.5 (C-3', C-4', C-5'), 22.9 ($NHCO\underline{C}H_3$), 22.1 (C-4), 21.1 (3 x $CO\underline{C}H_3$); HRMS calcd for $C_{25}H_{38}N_2O_{13}$ (M^+) 574.2374, found 574.2367. **33**: R_f 0.39 (20:1:1 EtOAc-acetone-hexanes, char A); mp 70-73 °C; $[\alpha]_D^{23}$ +46° (*c* 0.59, $CHCl_3$); IR ($CHCl_3$) 1745, 1665, 1515, 1220 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.54 (d, J = 8.1 Hz, NHAc), 5.94 (d, J = 7.8 Hz, 6-NH), 5.63 (s, H-2), 5.14 (m, H-6), 5.13 (s, H-1), 5.07 (dd, J = 7.7, 3.1 Hz, H-1"), 4.41 (dd, J = 12.0, 3.1 Hz, H-2"$_a$), 4.40 (m, H-2'), 4.09 (m, H-5), 4.06 (dd, J = 12.0, 7.8 Hz, H-2"$_b$), 3.82 (s, CO_2CH_3), 3.44 (s, OCH_3), 2.98 (m, H-1'), 2.10, 2.06, 2.04, 1.91 (s, 4 x $COCH_3$), 2.08-1.73 (m, H-4, H-3', H-4', H-5'); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 175.4, 170.9, 170.6, 170.3, 170.0 (6 x CO), 95.1 (C-1), 72.8 (C-3), 72.5 (C-1"), 72.1 (C-2), 67.0 (C-5), 62.4 (C-2"), 56.9, 54.2, 53.1 ($CO_2\underline{C}H_3$, C-1', C-2'), 52.8 (OCH_3), 47.6 (C-6), 30.2, 28.5, 28.0 (C-3', C-4', C-5'), 23.2 ($NHCO\underline{C}H_3$), 22.7 (C-4), 20.9, 20.9, 20.8 (3 x $CO\underline{C}H_3$); HRMS calcd for $C_{25}H_{38}N_2O_{13}$ (M^+) 574.2374, found 574.2403.

Methyl [(6*R)-6-[[((1'*R**,2'*S**) or (1'*S**,2'*R**)-2-Acetylaminocyclopentyl)-carbonyl]amino]-4,6-dideoxy-3-*C*-((1'*S**)-1,2-diacetyloxyethyl)]-α-D-xylo-heptopyranuronate, 1-Methyl-2-acetate (28), (29).** 85% combined yield. **28**: 43 % isolated yield; R_f 0.44 (20:1:1 EtOAc-acetone-hexanes, char A); mp 194-195 °C; $[\alpha]_D^{22}$ +13° (*c* 0.21, $CHCl_3$); IR ($CHCl_3$) 1745, 1660, 1525 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$, 55 °C) δ 6.34 (d, J = 9.1 Hz, NHAc), 6.00 (d, J = 8.4 Hz, 6-NH), 5.45 (dd, J = 7.6, 3.6 Hz, H-1"), 5.05 (d, J = 4.4, H-2), 4.89 (d, J = 4.1 Hz, H-1), 4.70-4.42 (m, H-2', H-5, H-6, H-2"$_a$), 4.13 (dd, J = 12.0, 7.6 Hz, H-2"$_b$), 3.77 (s, CO_2CH_3), 3.28 (s, OCH_3), 3.26 (m, H-1'), 2.07, 2.06, 2.03, 1.97 (s, 4 x $COCH_3$), 2.06-1.73 (m, H-4, H-3', H-4', H-5'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.6, 170.9, 170.6, 170.3 (6 x CO), 96.7 (C-1), 72.9 (C-1"), 71.9 (C-3), 70.2 (C-2), 67.2 (C-5), 62.8 (C-2"), 55.4, 54.6, 52.7 ($CO_2\underline{C}H_3$, C-1', C-2'), 52.4 (OCH_3), 49.2 (C-6), 34.6, 32.9, 27.6 (C-3', C-4', C-5'), 23.5 ($NHCO\underline{C}H_3$), 22.2 (C-4), 20.9, 20.8 (3 x $CO\underline{C}H_3$); HRMS calcd for $C_{25}H_{38}N_2O_{13}$ (M^+) 574.2374, found 574.2361. **29**: 42% isolated yield; R_f 0.41 (20:1:1 EtOAc-acetone-hexanes, char A); $[\alpha]_D^{22}$ -25.2° (*c* 1.39, $CHCl_3$); IR ($CHCl_3$) 1745, 1665, 1520 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.61 (d, J = 8.2 Hz, NHAc), 7.42 (d, J = 9.3 Hz, 6-NH), 5.26 (dd, J = 8.4, 2.8 Hz, H-1"), 5.14 (d, J = 4.9, H-2), 4.83 (d, J = 4.9 Hz, H-1),

4.63 (m, H-6, H-2"$_a$), 4.39, (m, H-2', H-5), 4.12 (dd, J = 12.1, 8.5 Hz, H-2"$_b$), 3.77 (s, CO_2CH_3), 3.20 (s, OCH_3), 3.01 (m, H-1'), 2.04, 2.03, 1.99, 1.91 (s, 4 x $COCH_3$), 2.11-1.47 (m, H-4, H-3', H-4', H-5'); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 174.7, 171.7, 180.0, 170.1, 170.0 (6 x CO), 96.4 (C-1), 72.7 (C-1"), 72.0 (C-3), 67.8 (C-2), 66.0 (C-5), 62.9 (C-2"), 55.7, 55.2, 53.1 ($CO_2\underline{C}H_3$, C-1', C-2'), 52.9 (OCH_3), 46.4 (C-6), 33.8, 30.3, 26.1 (C-3', C-4', C-5'), 22.7 ($NHCO\underline{C}H_3$), 21.6 (C-4), 20.8 (3 x $CO\underline{C}H_3$); HRMS calcd for $C_{25}H_{38}N_2O_{13}$ (M^+) 574.2374, found 574.2327.

General Procedure for Mosher Ester Synthesis. To a solution of alcohol **31**, DCC (1.1 equiv) and DMAP (0.01 equiv) in CH_2Cl_2 (0.1 M) was added a solution of (+)- or (-)-MTPA (1 equiv, 0.2 M in CH_2Cl_2). The reaction mixture was stirred at room temperature until judged complete by TLC (1 to 2 h). The reaction mixture was filtered, and filtrate was diluted with CH_2Cl_2 and washed sequentially with 1 N HCl, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$, then evaporated to give the crude Mosher ester. To avoid inadvertent enrichment, the crude ester was passed through a short column (SiO_2, 1:1 EtOAc-hexanes) to remove only those impurities which are either very polar (R_f< 0.1)or nonpolar (R_f> 0.9).

Methyl (6*R)-6-(tert-Butoxycarbonylamino)-6-[(*R**)-(α-methoxy-α-(trifluoromethyl)phenyl-acetoxymethyl]-4,6-dideoxy-3-*C*-(1'*S**)-1,2-diacetyloxyethyl)-α-D-glucopyranoside, 2-Acetate (34)**: 84% isolated yield; R_f 0.67 (2:1 EtOAc-hexanes, char A); $[\alpha]_D^{22}$ -13° (*c* 0.79, $CHCl_3$); ^1H NMR (200 MHz, C_6D_6, 60 °C) δ 7.64-7.07 (m, Ph), 5.46 (dd, J = 8.1, 2.9 Hz, H-1'), 5.41 (d, J = 1.7 Hz, H-2), 4.89 (d, J = 2.5 Hz, H-1), 4.71 (dd, J = 11.9, 3.0 Hz, H-2'$_a$), 4.56 (m, H-7$_a$), 4.39 (m, H-6), 4.28 (m, H-7$_b$), 4.20 (dd, J = 12.0, 8.0 Hz, H-2'$_b$), 3.69 (m, H-5), 3.37 (s, OCH_3), 3.19 (s, 1-OCH_3), 1.93, 1.85, 1.74 (s, 3 x OAc), 1.82 (m, H-4$_a$), 1.35 (s, BOC).

Methyl (6*R)-6-(tert-Butoxycarbonylamino)-6-[(*S**)-(α-methoxy-α-(trifluoromethyl)phenyl-acetoxymethyl]-4,6-dideoxy-3-*C*-(1'*S**)-1,2-diacetyloxyethyl)-α-D-glucopyranoside, 2-Acetate (35)**: 80% isolated yield; R_f 0.67 (2:1 EtOAc-hexanes, char A); $[\alpha]_D^{22}$ -21° (*c* 0.59, $CHCl_3$); ^1H NMR (200 MHz, C_6D_6, 60 °C) δ 7.64-7.07 (m, Ph), 5.44 (dd, J = 8.1, 2.8 Hz, H-1'), 5.42 (d, J = 2.1 Hz, H-2), 4.88 (d, J = 2.1 Hz, H-1), 4.70 (dd, J = 11.8, 2.8 Hz, H-2'$_a$), 4.53 (m, H-7$_a$), 4.43 (m, H-6), 4.33 (m, H-7$_b$), 4.20 (dd, J = 11.9, 8.1 Hz, H-2'$_b$), 3.78 (m, H-5), 3.43 (s, OCH_3), 3.17 (s, 1-OCH_3), 2.06 (dd, J = 14.8, 6.0 Hz, H-4$_a$), 1.93, 1.85, 1.74 (s, 3 x OAc), 1.82 (m, H-4$_a$), 1.35 (s, BOC).

ACKNOWLEDGEMENTS

This work was supported by Public Health Service Grant GM 35557 administered by the National Institute of General Medical Sciences.

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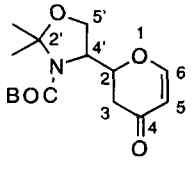
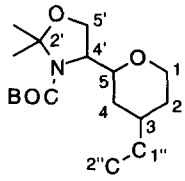
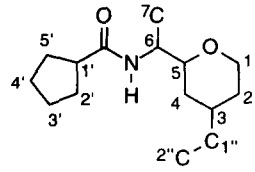
[20] Inquiries concerning this X-ray structure determination should be addressed to W. J. Y. at the Department of Chemistry, The University of Akron, Akron, OH 44325-3601. The atomic coordinates and thermal parameters for compound **31** will be deposited with the Cambridge Crystallographic Data Centre. These coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre. 12 Union Road, Cambridge, CB2 1EZ, UK.
[21] The numbering system used in this paper corresponds to the current CA index names for substructures **i-iii**. For details, see: Chemical Abstracts Service Index Guide; American Chemical Society: Washington, DC, 1989.



i



ii



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