General Approach to Hydroxylated α-Amino Acids Exploiting *N*-(*tert*-Butoxycarbonyl)-2-(*tert*-butyldimethylsiloxy)pyrrole

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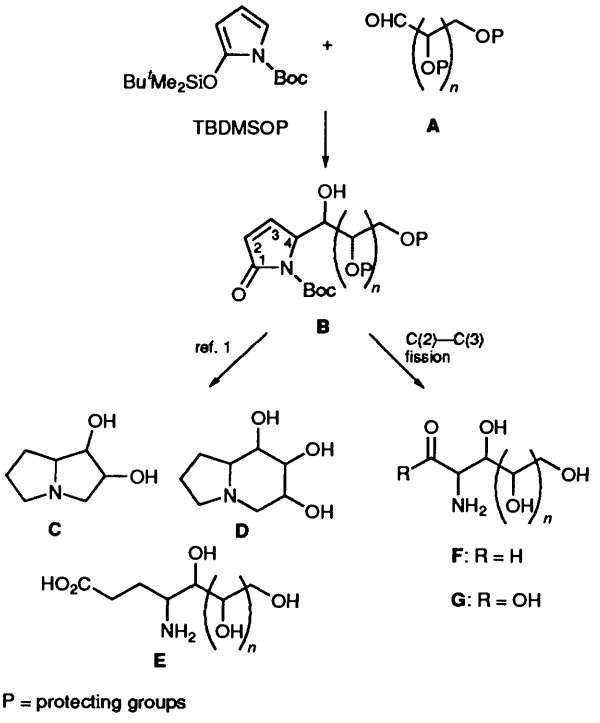
Racemic β-hydroxy-α-amino acids **7a**, **7b** and **10** of either *threo* or *erythro* configuration have been efficiently synthesized from simple aldehydes, utilizing *N*-(*tert*-butoxycarbonyl)-2-(*tert*-butyldimethylsiloxy)pyrrole (TBDMSOP) as a glycine-anion equivalent. Similar methodology, employing readily available aldehydo sugar precursors, has been successfully applied to syntheses of enantiomerically pure polyhydroxylated α-amino acids **14a–14f** possessing diverse constitution and chirality.

N-(*tert*-Butoxycarbonyl)-2-(*tert*-butyldimethylsiloxy)pyrrole (hereafter TBDMSOP) is a versatile four-carbon building block in organic synthesis for a masked pyrrolidine or γ-amino acid system.[1] As shown in Scheme 1, by reaction with homochiral



Scheme 1 Boc = *tert*-butoxycarbonyl

hydroxy aldehydes or aldehydo sugars of type **A**, TBDMSOP served to synthesize a variety of cyclic and open-chain oxygen- and nitrogen-containing compounds. Through the intermediacy of structurally defined α,β-unsaturated lactams **B**, pyrrolizidine and indolizidine derivatives **C** and **D**[1c,d] as well as polyhydroxylated γ-aminobutanoic acids **E**[1e] were stereospecifically generated, which incorporate the complete carbon skeleton and chirality of the respective lactam precursors.

Aiming at further exploration of the potential of TBDMSOP en route to biologically important hydroxylated and aminated compounds, we reasoned that oxidative extrusion of the C(1) and C(2) carbon atoms in the unsaturated lactam precursors **B** would provide a straightforward entry to hydroxylated α-amino aldehyde and α-amino acid derivatives **F** and **G**. In this paper,† we provide a full account of the stereoselective syntheses of racemic β-hydroxy-α-amino acids **7a**, **b** and **10** and enantiopure polyhydroxylated α-amino acids **14a–f** according to a two-carbon homologative protocol exploiting TBDMSOP as a novel glycine anion equivalent.

Results and Discussion

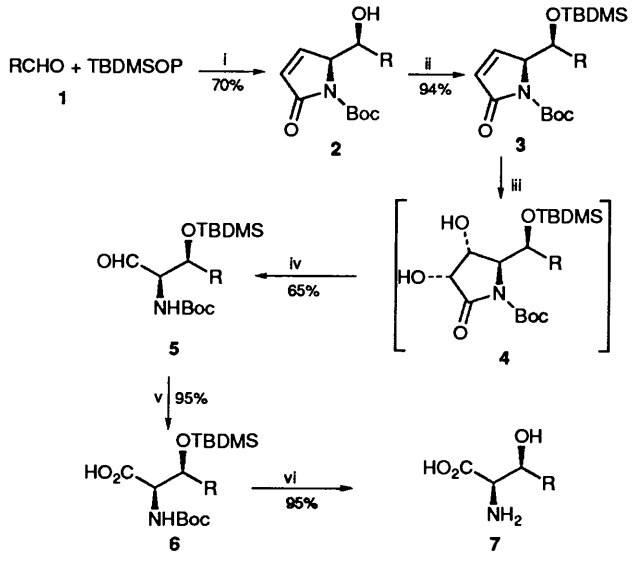
Synthesis of Racemic β-Hydroxy-α-amino Acids.—To evaluate the feasibility of the planned synthetic procedure, our first study was carried out in a racemic domain, utilizing acetaldehyde **1a** and isobutyraldehyde **1b** to create racemic threonine **7a** and *threo*-3-hydroxyleucine **7b**, respectively (Scheme 2).

Aldehydes **1a**, **b** were thus condensed with TBDMSOP by following our existing protocol ($SnCl_4$, Et_2O, −80 °C)[1a,b] to generate the respective *threo*-lactams **2a**, **b** almost exclusively (~70% yield). The stereochemistry of the coupling reaction was confirmed after the final amino acids were obtained by comparison with authentic samples. For lactams **2** to be converted into amino acids **7**, a clean protocol was envisaged consisting of three key reactions, namely, double-bond hydroxylation, fission of the C(2)–C(3) carbon bond to create an aldehyde function, and final oxidation to a carboxylic acid. This operational sequence allows isolation of useful α-amino aldehyde intermediates.

Protection of the free OH-function of compounds **2a**, **b** with *tert*-butyldimethylsilyl chloride (TBDMSCl)–imidazole generated silyl ethers **3a**, **b** (94%) which were subjected to double-bond hydroxylation using $KMnO_4$ under solid–liquid phase-transfer conditions.[3] Thus were obtained hydroxylated lactams **4a**, **b** which were directly converted into protected α-amino aldehydes **5a**, **b** by treatment with LiOH and tetrahydrofuran (THF) followed by oxidative fission of the formed open-chain diol ($NaIO_4$), in ~65% yield from lactams **3a**, **b**. Treatment of aldehydes **5a**, **b** with the $NaIO_4$–RuO_2 system gave protected amino acids **6a**, **b** (95–97% yield) which were finally transformed into free racemic threonine **7a** and *threo*-3-hydroxyleucine **7b** (95% each) by treatment with trifluoroacetic acid (TFA) and silica gel chromatography with CH_2Cl_2–methanolic ammonia as eluent.

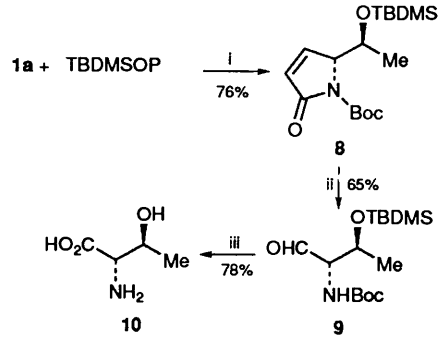
As previously reported,[1a] reversal of stereochemistry during

† Part of this work was published in a preliminary communication. See ref. 2.



a R = Me
b R = Pr^i
TBDMS = $SiMe_2Bu^t$; Boc = CO_2Bu^t

Scheme 2 *Reagents and conditions:* i, $SnCl_4$, Et_2O, −80 °C; ii, TBDMSCl, imidazole, DMF; iii, $KMnO_4$, DCH-18-crown-6, CH_2Cl_2; iv, aq. LiOH, THF, 0 °C; then aq. $NaIO_4$, SiO_2, CH_2Cl_2; v, $NaIO_4$, RuO_2, CCl_4–MeCN–aq. acetone; vi, TFA, MeOH; then SiO_2 chromatogr., CH_2Cl_2–MeOH–aq. NH_4OH



Scheme 3 *Reagents and conditions:* i, BF_3·OEt_2, Et_2O, −80 °C; then TBDMSCl, imidazole, DMF; ii, $KMnO_4$, DCH-18-crown-6, CH_2Cl_2; then aq. LiOH, THF, 0 °C; then aq. $NaIO_4$, SiO_2, CH_2Cl_2; iii, $NaIO_4$, RuO_2, CCl_4–MeCN–aq. acetone; then TFA, MeOH; then SiO_2 chromatogr., CH_2Cl_2–MeOH–aq. NH_4OH

the aldehyde–TBDMSOP coupling to generate *erythro*-lactams can be attained by changing the Lewis acid promoter to BF_3–diethyl ether. Scheme 3 illustrates how allothreonine **10** was synthesized. BF_3-promoted condensation of acetaldehyde **1a** with TBDMSOP and subsequent silylation gave rise to protected *erythro*-lactam **8** (76%), which was converted into racemic acid **10**, by following the protocol used for compound **7**, in 50% overall yield for the entire sequence. Only lactam **8** and aldehyde **9** were isolated in a pure state and fully characterized, resulting in improved yield and reduced synthetic effort.

Synthesis of Polyhydroxylated α-Amino Acids.—With an efficient scheme to convert simple aldehydes into racemic hydroxylated α-amino acids in hand, we set out to explore its utility in asymmetric synthesis. In this context, readily available open-chain sugar aldehydes were envisaged as ideal precursors for polyhydroxy-α-amino acids, a family of compounds strictly related to naturally occurring (+)-polyoxamic acid and polyoxin complex.[4] Successful implementation of this strategy to chiral syntheses of five-, six-, and seven-carbon 2-deoxy-2-aminoaldonic acids **14a–f** was easily attained starting from enantiomerically pure aldehydes **11a–e**. The resulting amino acids and the major reaction intermediates are shown in Table 1.

The overall sequence consisted of three consecutive operations: (i) condensation and protection to give lactams **12**; (ii) *cis*-dihydroxylation, ring opening, and cleavage of the diol bond to give aminoaldoses **13**; and (iii) oxidation–deprotection to give aminoaldonic acids **14**. Transformations in entries 1–4 and 6 followed exactly the same chemistry as used for racemic amino acids **7a**, **b** and **10**, while preparation of L-aminogalactonic acid **14e** (entry 5) required a slightly modified deprotection procedure. Since treatment of compound **13e** with $NaIO_4$–RuO_2 caused concomitant oxidation of the terminal *O*-benzyl group to benzoyl, debenzoylation had to be performed (MeOH, MeONa) in addition to the usual acidic treatment (see Experimental section).

It is worth noting that amino acids **14a–e** (entries 1–5) invariably possess the 2,3-*threo*-3,4-*erythro* relative configuration, *i.e.* the same stereochemistry as the parent lactams **12a–e**. When $SnCl_4$ is used as a promoter in the condensation steps (**11a–e** ⟶ **12a**, **e**), 2*R*-configured aldehydes **11** predictably generate 2*S*-amino acids **14** (entries 1, 4, 5), while 2*S*-configured aldehydes **11** create 2*R*-amino acids **14** (entries 2 and 3). In contrast, as exemplified in entry 6, for BF_3-assisted condensation processes (*e.g.* **11a** to **12f**) 2*R*-aldehydes produce 2*R*-amino acids (*e.g.*, **14f**) with 2,3-*erythro*-3,4-*erythro* relative configurations.

The absolute stereochemistries of both the final amino acids **14** and the pertinent intermediates **12** and **13** were established as shown based on the chirality of the lactam precursors and the observed stereoconservative behaviour of the transformation sequences. The structural assignments of unsaturated lactams **12a** (and hence **12b**),[1b] **12e**,[1b] and **12f**[1d] were secured by single-crystal X-ray analyses on derivatives, as reported in the previous papers of this series. The chirality of arabinose-based lactams **12c**, **d** was tentative and supported by analogy considerations.*

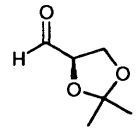
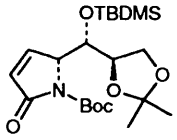
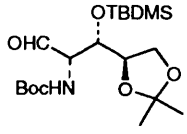
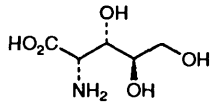
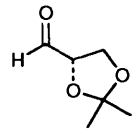
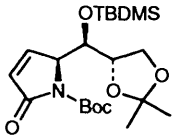
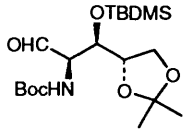
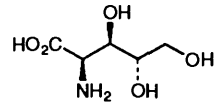
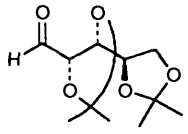
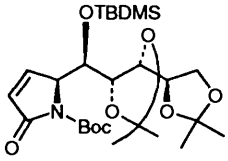
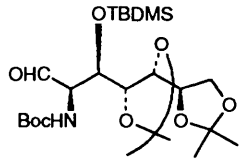
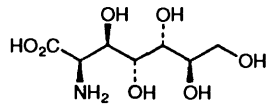
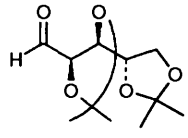
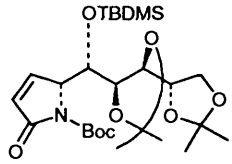
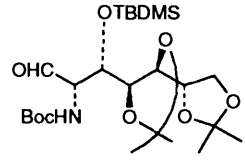
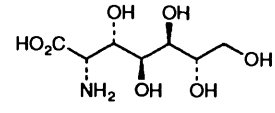
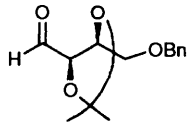
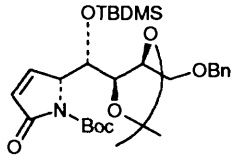
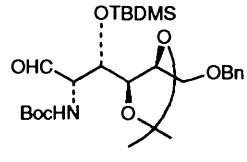
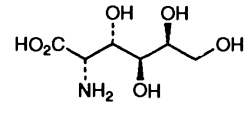
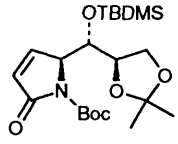
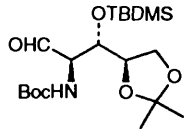
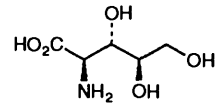
Conclusions.—The protocol outlined in this paper establishes a practical and convenient access to a wide range of hydroxylated α-amino acids, while meeting such important criteria as high selectivity, flexibility and predictable stereocontrol. Not only does its applicability encompass the preparation of hydroxylated α-amino acids, but it also appears suitable, at least in principle, for extension to many other members of the non-proteinaceous amino acids domain.[6]

Experimental

M.p.s were determined on an Electrothermal apparatus and were recorded uncorrected. ^1H and ^{13}C NMR spectra were recorded on a Varian XL-300 or a Bruker AC-300 instrument. *J* Values are given in Hz, and chemical shifts are referenced to tetramethylsilane (δ 0.0), DOH (δ 4.80), or CD_3OD (δ_H 3.35 and δ_C 49.0). High-resolution mass spectra were recorded on a Kratos Concept 1-S instrument under chemical-ionization (CI) conditions using methane. After aqueous work-up of reaction mixtures, organic solutions were routinely dried with magnesium sulfate, and 'evaporation' or 'evaporated' refers to removal of solvent on a rotary apparatus. TLC was carried out on Merck Kieselgel 60 F_{254} glass-backed plates. The plates were visualized by dipping in a solution of Ce^{III} sulfate–ammonium molybdate–sulfuric acid or in an ethanolic solution of ninhydrin, followed by heating. Silica gel (particle size 70–230 mesh)

* As a rule, irrespective of the nature and chirality of the substituents, 4*R*-configured γ-lactams of this series are dextrorotatory, while 4*S*-compounds are laevorotatory. The same correlation was observed for a series of γ-lactone analogues. See ref. 5.

Table 1 Synthesis of polyhydroxy-α-amino acids **14a–f**[a]

Entry	Aldehyde precursor	Unsaturated lactam	Amino aldehyde	Amino acid	Overall yield (%)
1	 **11a**	 **12a** (78%)	 **13a** (60%)	 **14a** (76%)	36
2	 **11b**	 **12b** (80%)	 **13b** (64%)	 **14b** (81%)	42
3	 **11c**	 **12c** (75%)	 **13c** (61%)	 **14c** (84%)	39
4	 **11d**	 **12d** (81%)	 **13d** (66%)	 **14d** (79%)	42
5	 **11e**	 **12e** (70%)	 **13e** (61%)	 **14e** (74%)	32
6	**11a**	 **12f** (67%)	 **13f** (60%)	 **14f** (80%)	32

[a] *Reagents and conditions:* **11a–e→12a–e**, $SnCl_4$, Et_2O, −80 °C; then TBDMSCl, imidazole, DMF; **11a→12f**, $BF_3{\cdot}OEt_2$, Et_2O, −80 °C; then TBDMSCl, imidazole, DMF; **12a–f→13a–f**, $KMnO_4$, DCH-18-crown-6, CH_2Cl_2; then aq. LiOH, THF, O °C; then aq. $NaIO_4$, SiO_2, CH_2Cl_2; **13a–d→14a–d** and **13f→14f**, $NaIO_4$, RuO_2, CCl_4–MeCN–aq. acetone; then TFA, MeOH; then SiO_2 chromatogr., CH_2Cl_2–MeOH–aq. NH_4OH; **13e→14e**, $NaIO_4$, RuO_2, CCl_4–MeCN–aq. acetone; then NaOMe, MeOH; then TFA, MeOH; then SiO_2 chromatogr., CH_2Cl_2–MeOH–aq. NH_4OH.

supplied by Merck was employed for flash chromatography.[7] $[\alpha]_D$ Values were measured on a Perkin-Elmer 241 polarimeter and are given in units of 10^{-1} deg cm^2 g^{-1}. Elemental analyses were performed by the Microanalytical Laboratory of the University of Sassari. *N*-(*tert*-Butoxycarbonyl)-2-(*tert*-butyldimethylsiloxy)pyrrole (TBDMSOP) was prepared from pyrrole according to a described protocol.[1a] 2,3-*O*-Isopropylidene-D- and -L-glyceraldehyde **11a** and **11b**,[8,9] 2,3:4,5-di-*O*-isopropylidene-D-and -L-arabinose **11c** and **11d**,[10] and 4-*O*-benzyl-2,3-*O*-isopropylidene-L-threose **11e**[3] were prepared according to literature methods.

(±)-threo-4-(tert-*Butoxycarbonylamino*)-5-*hydroxyhex*-2-*enoic Acid* 1,4-*Lactam* **2a**.—*Typical procedure*. TBDMSOP (5.0 g, 16.9 mmol) and acetaldehyde **1a** (0.79 cm^3, 14.0 mmol) were dissolved in anhydrous Et_2O (100 cm^3) under nitrogen and the mixture was cooled to −80 °C. $SnCl_4$ (2.5 cm^3, 21.1 mmol) was added dropwise during 5 min and the solution was stirred for 4 h. The reaction was quenched at this temperature by addition of an excess of saturated aq. $NaHCO_3$. The mixture was warmed to room temperature and extracted with Et_2O (3 × 30 cm^3). The organic layer was evaporated to give the crude lactam, which was purified by flash chromatography over silica gel and

eluted with 60:40 EtOAc–hexane to afford pure *lactam* **2a** (3.12 g, 70%) as a glassy solid (Found: C, 58.3; H, 7.4; N, 6.0. $C_{11}H_{17}NO_4$ requires C, 58.1; H, 7.5; N, 6.2%); δ_H(300 MHz; $CDCl_3$) 1.02 (3 H, d, *J* 6.6, Me), 1.56 (9 H, s, Bu^t), 3.54 (1 H, br s, OH), 4.49 (1 H, m, 5-H), 4.77 (1 H, ddd, *J* 5.4, 2.1 and 1.8, 4-H), 6.19 (1 H, dd, *J* 6.3 and 1.8, 2-H) and 7.35 (1 H, dd, *J* 6.3 and 2.1, 3-H); δ_C(75.4 MHz; $CDCl_3$) 16.9, 28.0 (3 C), 66.9, 67.1, 83.5, 127.6, 148.6, 150.1 and 169.5.

(±)-threo-4-(tert-*Butoxycarbonylamino*)-5-*hydroxy*-6-*methylhept*-2-*enoic Acid* 1,4-*Lactam* **2b**.—The *title compound* was prepared by starting with isobutyraldehyde **1b** (0.51 cm^3, 5.6 mmol) following the procedure described for lactam **2a**, and was obtained as an oil (1.0 g, 70%) (Found: C, 61.3; H, 8.1; N, 5.4. $C_{13}H_{21}NO_4$ requires C, 61.2; H, 8.3; N, 5.5%); δ_H(300 MHz; $CDCl_3$) 0.90 (3 H, d, *J* 6.4, 7-H_3), 0.91 (3 H, d, *J* 6.8, 6-Me), 1.52 (9 H, s, Bu^t), 1.63 (1 H, m, 6-H), 3.73 (2-H, m, 5-H and OH), 4.73 (1 H, m, 4-H), 6.08 (1 H, dd, *J* 6.2 and 1.7, 2-H) and 7.27 (1 H, dd, *J* 6.2 and 2.0, 3-H).

(±)-threo-4-(tert-*Butoxycarbonylamino*)-5-(tert-*butyldimethylsiloxy*)*hex*-2-*enoic Acid* 1,4-*Lactam* **3a**.—*Typical procedure*. To a solution of **2a** (2.7 g, 12.0 mmol) in dry dimethylformamide (DMF) (80 cm^3) were added TBDMSCl (18.0 g, 120 mmol) and imidazole (8.1 g, 120 mmol) and the mixture was stirred at room temperature for 4 h before being poured into 5% aq. citric acid (200 cm^3), and the resulting slurry was extracted with Et_2O (3 × 50 cm^3). The extracts were evaporated and crude lactam **3a** was purified by flash chromatography on silica gel and eluted with 70:30 hexane–EtOAc to afford pure *siloxy lactam* **3a** (3.85 g, 94%) as an oil (Found: C, 59.9; H, 9.0; N, 4.0. $C_{17}H_{31}NO_4Si$ requires C, 59.8; H, 9.2; N, 4.1%); δ_H(300 MHz; $CDCl_3$) 0.09 (3 H, s, Me), 0.12 (3 H, s, Me), 0.85 (3 H, d, *J* 5.9, 6-H_3), 0.90 (9 H, s, Bu^t), 1.54 (9 H, s, Bu^t), 4.60 (2 H, m, 4- and 5-H), 6.16 (1 H, dd, *J* 5.6 and 1.0, 2-H) and 7.26 (1 H, dd, *J* 5.6 and 1.3, 3-H); δ_C(75.4 MHz; $CDCl_3$) −5.0, −4.9, 16.3, 17.8, 25.6 (3 C), 28.0 (3 C), 66.3, 67.0, 82.9, 127.6, 148.8, 151.5 and 169.5.

(±)-threo-4-(tert-*Butoxycarbonylamino*)-5-(tert-*butyldimethylsiloxy*)-6-*methylhept*-2-*enoic Acid* 1,4-*Lactam* **3b**.—The *title compound* was prepared by starting with compound **2b** (0.88 g, 3.4 mmol) following the procedure described for compound **3a**, and was obtained as an oil (11.8 g, 94%) (Found: C, 61.9; H, 9.9; N, 3.6. $C_{19}H_{35}NO_4Si$ requires C, 61.8; H, 9.6; N, 3.8%); δ_H(300 MHz; $CDCl_3$) 0.10 (3 H, s, Me), 0.15 (3 H, s, Me), 0.88 (9 H, s, Bu^t), 0.93 (6 H, m, 6-Me_2), 1.50 (1 H, m, 6-H), 1.54 (9 H, s, Bu^t), 4.60 (2 H, m, 4- and 5-H), 6.11 (1 H, dd, *J* 6.0 and 1.6, 2-H) and 7.36 (1 H, dd, *J* 6.0 and 1.7, 3-H); δ_C(75.4 MHz; $CDCl_3$) −3.6 (2 C), 17.7, 18.1, 25.3 (3 C), 25.5 (2 C), 27.9 (3 C), 66.5, 74.8, 82.0, 126.4, 149.5, 151.0 and 164.5.

(±)-threo-2-(tert-*Butoxycarbonylamino*)-3-(tert-*butyldimethylsiloxy*)*butanal* **5a**.—*Typical procedure*. To a stirred solution of lactam **3a** (2.75 g, 8.0 mmol) in anhydrous CH_2Cl_2 (50 cm^3) were added dicyclohexano-18-crown-6 ether (0.4 g, 1.0 mmol) and powdered $KMnO_4$ (0.5 g, 3.0 mmol) at room temperature. After 30 min the slurry mixture was filtered through a Celite pad and the filtrates were evaporated to give crude diol **4a**, which was purified by flash chromatography and eluted with 70:30 EtOAc–hexane.

Lactam **4a** was directly dissolved in THF (50 cm^3) and 1 mol dm^{-3} aq. LiOH (35 cm^3) was added to the stirred solution at 0 °C. After 30 min the solvent was removed and the residue was dissolved in CH_2Cl_2 (120 cm^3). SiO_2 (230–400 mesh, 10 g) was added and the resulting, vigorously stirred slurry was treated with 0.65 mol dm^{-3} aq. $NaIO_4$ (20 cm^3) at room temperature. After 15 min the slurry was filtered under suction and the silica was thoroughly washed with CH_2Cl_2. The filtrates were evaporated to leave crude aldehyde **5a**, which was finally purified by flash chromatography on silica gel and eluted with 70:30 hexane–EtOAc to give an oil (1.65 g, 65%) (Found: C, 56.6; H, 9.6; N, 4.3. $C_{15}H_{31}NO_4Si$ requires C, 56.7; H, 9.8; N, 4.4%); δ_H(300 MHz; $CDCl_3$) 0.36 (3 H, s, Me), 0.57 (3 H, s, Me), 0.84 (9 H, s, Bu^t), 1.17 (3 H, d, *J* 6.2, 4-H_3), 1.45 (9 H, s, Bu^t), 4.16 (1 H, dd, *J* 8.0 and 2.6, 2-H), 4.48 (1 H, dq, *J* 6.2 and 2.6, 3-H), 5.26 (1 H, d, *J* 8.0, NH) and 9.64 (1 H, br s, 1-H); δ_C(75.4 MHz; $CDCl_3$) −4.5 (2 C), 17.7, 20.1, 25.6 (3 C), 28.2 (3 C), 65.1, 67.1, 79.9, 156.0 and 200.8.

(±)-threo-2-(tert-*Butoxycarbonylamino*)-3-(tert-*butyldimethylsiloxy*)-4-*methylpentanal* **5b**.—The *title compound* was prepared by starting with lactam **3b** (0.8 g, 2.1 mmol) following the procedure described for compound **5a**, and gave aldehyde **5b** as an oil (0.47 g, 65%) (Found: C, 59.2; H, 10.0; N, 4.0. $C_{17}H_{35}NO_4Si$ requires C, 59.1; H, 10.2; N, 4.1%); δ_H(300 MHz; $CDCl_3$) 0.07 (6 H, s, Me), 0.88 (9 H, s, Bu^t), 0.91 (3 H, d, *J* 6.7, 5-H_3), 0.92 (3 H, d, *J* 7.0, 4-Me), 1.46 (9-H, s, Bu^t), 1.67 (1 H, m, 4-H), 4.04 (1 H, d, *J* 3.8, 2-H), 4.20 (1 H, dd, *J* 5.8 and 2.2, 3-H), 5.29 (1 H, d, *J* 6.7, NH) and 9.65 (1 H, br s, 1-H); δ_C(75.4 MHz; $CDCl_3$) −4.6, −4.5, 18.0, 18.3, 18.4, 25.7 (3 C), 28.2 (3 C), 32.3, 61.8, 68.0, 80.0, 151.0 and 202.3.

(±)-N-(tert-*Butoxycarbonyl*)-3-O-(tert-*butyldimethylsilyl*)-*threonine* **6a**.—*Typical procedure*. Protected aldehyde **5a** (1.6 g, 5.0 mmol) was dissolved in a MeCN (20 cm^3)–CCl_4 (20 cm^3)–water (28 cm^3)–acetone (5 cm^3) stirred solvent mixture and treated with solid $NaIO_4$ (4.28 g, 20 mmol) at room temperature. After 15 min, hydrated RuO_2 (20 mg) was added and the mixture was stirred for a further 1 h. The mixture was treated with propan-2-ol (5 cm^3) and filtered through a Celite pad. The solvent was removed and the residue was chromatographed over silica gel (70:30 EtOAc–hexane) to give *protected threonine* **6a** (1.58 g, 95%) as an oil (Found: C, 54.1; H, 9.2; N, 4.1. $C_{15}H_{31}NO_5Si$ requires C, 54.0; H, 9.4; N, 4.2%); δ_H(300 MHz; CD_3OD) 0.05 (3 H, s, Me), 0.08 (3 H, s, Me), 0.88 (9 H, s, Bu^t), 1.19 (3 H, d, *J* 6.2, 4-H_3), 1.46 (9 H, s, Bu^t), 4.08 (1 H, m, 2-H) and 4.45 (1 H, dq, *J* 6.2 and 2.1, 3-H); δ_C(75.4 MHz; CD_3OD) −5.0, −4.3, 18.8, 21.3, 26.2 (3 C), 28.6 (3 C), 60.6, 70.1, 80.6, 130.0 and 174.2.

(±)-threo-N-(tert-*Butoxycarbonyl*)-3-(tert-*butyldimethylsiloxy*)*leucine* **6b**.—The *title compound* was prepared by starting with aldehyde **5b** (0.32 g, 0.93 mmol) following the procedure described for compound **6a**, to give solid compound **6b** (0.32 g, 95%), m.p. 130–133 °C (Found: C, 56.3; H, 9.6; N, 3.7. $C_{17}H_{35}NO_5Si$ requires C, 56.5; H, 9.8; N, 3.9%); δ_H(300 MHz; CD_3OD) 0.09 (6 H, s, Me), 0.91 (9 H, s, Bu^t), 0.94 (3 H, d, *J* 6.9, 5-H_3), 0.99 (3 H, d, *J* 6.7, 4-Me), 1.46 (9 H, s, Bu^t), 1.81 (1 H, app. oct, *J* 6.7, 4-H), 4.00 (1 H, dd, *J* 6.3 and 1.5, 3-H) and 4.27 (1 H, m, 2-H); δ_C(75.4 MHz; CD_3OD) −4.3, −4.2, 18.4, 19.4 (2 C), 26.3 (3 C), 28.5 (3 C), 34.0, 60.3, 72.0, 78.4, 150.0 and 173.2.

(±)-*Threonine* **7a**.—*Typical procedure*. Protected amino acid **6a** (1.0 g, 3.0 mmol) was dissolved in methanol (5 cm^3) and treated with TFA (3 cm^3) at room temperature. After being stirred for 1 h, the mixture was evaporated and the residue was subjected to flash chromatographic purification on silica gel and eluted with 6:4:1 CH_2Cl_2–MeOH–30% aq. NH_4OH. Removal of the solvent furnished pure racemic threonine **7a** (0.34 g, 95%) as crystals, m.p. 242 °C (decomp.) [lit.,[11] 244 °C (decomp.)]; δ_H(300 MHz; D_2O) 1.32 (3 H, d, *J* 6.5, 4-H_3), 3.54 (1 H, d, *J* 4.8, 2-H) and 4.23 (1 H, dq, *J* 6.5 and 4.8, 3-H); δ_C(75.4 MHz; D_2O) 20.4, 64.2, 69.6 and 172.9.

(±)-threo-3-*Hydroxyleucine* **7b**.—The title compound was prepared by starting with compound **6b** (0.3 g, 0.83 mmol)

following the procedure described for threonine **7a**, to give compound **7b** as a solid (0.12 g, 95%), m.p. 220–223 °C (lit.,[12] 222–223 °C); δ_H(300 MHz; D_2O) 0.79 (3 H, d, *J* 6.6, 5-H_3), 0.84 (3 H, d, *J* 6.6, 4-Me), 1.58 (1 H, app. oct, *J* 7.2, 4-H), 3.60 (1 H, dd, *J* 7.8 and 3.9, 3-H) and 3.66 (1 H, d, *J* 3.9, 2-H); δ_C(75.4 MHz; D_2O) 18.4, 19.4, 31.3, 58.0, 76.1 and 174.4.

(±)-erythro-4-(tert-*Butoxycarbonylamino*)-5-(tert-*butyldimethylsiloxy*)*hex*-2-*enoic Acid* 1,4-*Lactam* **8**.—*Typical procedure*. To a solution of TBDMSOP (2.0 g, 6.7 mmol) in anhydrous Et_2O (30 cm^3) were added acetaldehyde **1a** (0.5 cm^3, 8.8 mmol) and BF_3·OEt_2 (1.1 cm^3, 8.4 mmol) under nitrogen at −85 °C. The solution was stirred at this temperature for 4 h, then saturated aq. $NaHCO_3$ was added and, after ambient temperature was reached, the resulting mixture was extracted with Et_2O (3 × 20 cm^3). The solvent was evaporated off and the crude lactam intermediate was purified by flash chromatography on silica gel and eluted with 60:40 EtOAc–hexane.

This compound (1.2 g, 5.3 mmol) was directly subjected to silylation as described for lactam **3a** giving *protected lactam* **8** as an oil (1.74, 76%) (Found: C, 59.6; H, 9.1; N, 3.9. $C_{17}H_{31}NO_4Si$ requires C, 59.8; H, 9.2; N, 4.1%); δ_H(300 MHz; $CDCl_3$) 0.03 (6 H, s, Me), 0.77 (9 H, s, Bu^t), 1.27 (3 H, d, *J* 6.4, Me), 1.53 (9 H, s, Bu^t), 4.46 (1 H, ddd, *J* 2.0, 2.0, and 1.7, 4-H), 4.49 (1 H, dq, *J* 6.4 and 2.0, 5-H), 6.08 (1 H, dd, *J* 6.2 and 1.7, 2-H) and 7.15 (1 H, dd, *J* 6.2 and 2.0, 3-H); δ_C(75.4 MHz; $CDCl_3$) −5.4, −5.0, 17.7, 17.8, 25.5 (3 C), 28.0 (3 C), 66.2, 68.0, 82.7, 127.7, 146.7, 148.7 and 169.0.

(±)-erythro-2-(tert-*Butoxycarbonylamino*)-3-(tert-*butyldimethylsiloxy*)*butanal* **9**.—The *title compound* was prepared by starting with lactam **8** (1.5 g, 4.4 mmol) following the procedure described for aldehyde **5a**. Compound **9** was an oil (0.91 g, 65%) (Found: C, 56.6; H, 9.7; N, 4.2. $C_{15}H_{31}NO_4Si$ requires C, 56.7; H, 9.8; N, 4.4%); δ_H(300 MHz; $CDCl_3$) 0.02 (3 H, s, Me), 0.03 (3 H, s, Me), 0.84 (9 H, s, Bu^t), 1.21 (3 H, d, *J* 5.5, 4-H_3), 1.44 (9 H, s, Bu^t), 3.61 (1 H, m, 2-H), 4.18 (1 H, m, 3-H), 5.41 (1 H, br s, NH) and 9.78 (1 H, s, 1-H); δ_C(75.4 MHz; $CDCl_3$) −0.7, 0.6, 20.0, 21.7, 27.4 (3 C), 66.0, 71.0, 78.3, 162.1 and 197.5.

(±)-*Allothreonine* **10**.—The title compound was prepared by starting with aldehyde **9** (0.8 g, 2.5 mmol) by sequential execution of the procedures described for acids **6a** and **7a**. Compound **10** was obtained as a solid (0.23 g, 78%), m.p. 255 °C [lit.,[11] 252–253 °C (decomp.)]; δ_H(300 MHz; D_2O) 1.12 (3 H, d, *J* 6.6, 4-H_3), 3.76 (1 H, d, *J* 3.9, 2-H) and 4.29 (1 H, dq, *J* 6.6 and 3.9, 3-H); δ_C(75.4 MHz; D_2O) 17.1, 60.7, 66.3 and 172.3.

4-(tert-*Butoxycarbonylamino*)-5-O-(tert-*butyldimethylsilyl*)-2,3,4-*trideoxy*-6,7-O-*isopropylidene*-D-arabino-*hept*-2-*enonic Acid* 1,4-*Lactam* **12a**.—The *title compound* was prepared from aldehyde **11a** (1.3 g, 10 mmol) by following sequentially the procedures described for compounds **2a** and **3a**; compound **12a** was obtained as crystals (3.3 g, 78%), m.p. 140–142 °C, $[\alpha]_D$ +180.4 (*c* 0.92, $CHCl_3$) (Found: C, 58.8; H, 8.7; N, 3.2. $C_{21}H_{37}NO_6Si$ requires C, 59.0; H, 8.7; N, 3.3%); δ_H(300 MHz; $CDCl_3$) 0.16 (3 H, s, Me), 0.21 (3 H, s, Me), 0.93 (9 H, s, Bu^t), 1.24 (3 H, s, Me), 1.35 (3 H, s, Me), 1.58 (9 H, s, Bu^t), 3.6–3.8 (3 H, m, 6-H and 7-H_2), 4.60 (1 H, br t, *J* 4.5, 5-H), 4.65 (1 H, m, 4-H), 6.20 (1 H, dd, *J* 6.0 and 1.5, 2-H) and 7.28 (1 H, dd, *J* 6.0 and 2.1, 3-H); δ_C(75.4 MHz; $CDCl_3$) −0.5, −0.4, 17.9, 25.0, 25.7 (3 C), 26.3, 28.2 (3 C), 65.2, 66.1, 71.2, 74.7, 83.2, 109.0, 128.4, 147.4, 149.3 and 169.0.

The following lactams were obtained from the respective aldehyde precursors by essentially the same procedure:

4-(tert-*Butoxycarbonylamino*)-5-O-(tert-*butyldimethylsilyl*)-2,3,4-*trideoxy*-6,7-O-*isopropylidene*-L-arabino-*hept*-2-*enonic acid* 1,4-*lactam* **12b**. From aldehyde **11b** (1.3 g, 10 mmol) as crystals (3.4 g, 80%), m.p. 138–140 °C; $[\alpha]_D$ −178.6 (*c* 0.8, $CHCl_3$) (Found: C, 59.1; H, 8.5; N, 3.0%); ^1H and ^{13}C NMR, see compound **12a**.

4-(tert-*Butoxycarbonylamino*)-5-O-(tert-*butyldimethylsilyl*)-2,3,4-*trideoxy*-6,7:8,9-*di*-O-*isopropylidene*-D-glycero-D-galacto-*non*-2-*enonic acid* 1,4-*lactam* **12c**. From aldehyde **11c** (1.15 g, 5 mmol), as an oil (1.98 g, 75%), $[\alpha]_D$ −85.6 (*c* 3.2, $CHCl_3$) (Found: C, 59.0; H, 8.4; N, 2.4. $C_{26}H_{45}NO_8Si$ requires C, 59.2; H, 8.6; N, 2.7%); δ_H(300 MHz; $CDCl_3$) 0.21 (3 H, s, Me), 0.26 (3 H, s, Me), 0.95 (9 H, s, Bu^t), 1.27 (3 H, s, Me), 1.28 (3 H, s, Me), 1.29 (3 H, s, Me), 1.32 (3 H, s, Me), 1.56 (9 H, s, Bu^t), 3.41 (1 H, dd, *J* 8.4 and 5.7), 3.84 (1 H, t, *J* 7.5), 3.95 (1 H, dd, *J* 7.8 and 6.3), 4.16 (2 H, m), 4.52 (1 H, dd, *J* 8.4 and 4.5), 4.68 (1 H, ddd, *J* 4.2, 1.8, and 1.5, 4-H), 6.22 (1 H, dd, *J* 6.0 and 1.5, 2-H) and 7.30 (1 H, dd, *J* 6.0 and 1.8, 3-H); δ_C(75.4 MHz; $CDCl_3$) −4.7, −4.3, 17.9, 25.3, 25.7 (3 C), 26.3, 27.2, 27.5, 28.2 (3 C), 64.9, 65.5, 71.6, 76.0, 78.0, 79.4, 82.8, 109.2, 110.7, 128.9, 146.7, 149.7 and 168.7.

4-(tert-*Butoxycarbonylamino*)-5-O-(tert-*butyldimethylsilyl*)-2,3,4-*trideoxy*-6,7:8,9-*di*-O-*isopropylidene*-L-glycero-L-galacto-*non*-2-*enonic acid* 1,4-*lactam* **12d**. From aldehyde **11d** (0.92 g, 4 mmol), as an oil (1.7 g, 81%), an oil; $[\alpha]_D$ +85.1 (*c* 5.8 in $CHCl_3$) (Found: C, 59.4; H, 8.4; N, 2.5%); ^1H and ^{13}C NMR, see compound **12c**.

8-O-*Benzyl*-4-(tert-*butoxycarbonylamino*)-5-O-(tert-*butyldimethylsilyl*)-2,3,4-*trideoxy*-6,7-O-*isopropylidene*-L-galacto-*oct*-2-*enonic acid* 1,4-*lactam* **12e**. From aldehyde **11e** (1.25 g, 5 mmol), as an oil (1.92 g, 70%), $[\alpha]_D$ +108.6 (*c* 3.4, $CHCl_3$) (Found: C, 63.5; H, 8.1; N, 2.5. $C_{29}H_{45}NO_7Si$ requires C, 63.6; H, 8.3; N, 2.6%); δ_H(300 MHz; $CDCl_3$) 0.12 (3 H, s, Me), 0.23 (3 H, s, Me), 0.88 (9 H, s, Bu^t), 1.30 (3 H, s, Me), 1.34 (3 H, s, Me), 1.56 (9 H, s, Bu^t), 3.3–3.5 (2 H, m), 3.61 (1 H, dd, *J* 10.2 and 2.1), 3.74 (1 H, m), 4.10 (1 H, td, *J* 7.2 and 1.8), 4.5–4.6 (2 H, m), 4.64 (1 H, td, *J* 4.8 and 1.8), 6.19 (1 H, dd, *J* 6.0 and 1.5, 2-H), 7.21 (1 H, dd, *J* 6.0 and 1.8, 3-H) and 7.3 (5 H, m, Ph); δ_C(75.4 MHz; $CDCl_3$) −4.7, −4.4, 17.7, 25.6 (3 C), 26.6, 26.8, 28.2 (3 C), 65.3, 71.4, 72.2, 73.4, 75.7, 79.9, 82.6, 110.1, 127.5, 127.7 (2 C), 128.2 (2 C), 128.9, 137.9, 146.5, 149.3 and 168.6.

(tert-*Butoxycarbonylamino*)-5-O-(tert-*butyldimethylsilyl*)-2,3,4-*trideoxy*-6,7-O-*isopropylidene*-D-ribo-*hept*-2-*enonic acid* 1,4-*lactam* **12f**. The *title compound* was prepared from aldehyde **11a** (0.8 g, 6 mmol) by following the procedure described for lactam **8**, and was obtained as an oil (1.72 g, 67%), $[\alpha]_D$ −82.2 (*c* 2.3, $CHCl_3$) (Found: C, 58.7; H, 8.7; N, 3.2. $C_{21}H_{37}NO_6Si$ requires C, 59.0; H, 8.7; N, 3.3%); δ_H(300 MHz; $CDCl_3$) −0.01 (3 H, s, Me), 0.03 (3 H, s, Me), 0.79 (9 H, s, Bu^t), 1.38 (3 H, s, Me), 1.47 (3 H, s, Me), 1.57 (9 H, s, Bu^t), 3.85 (1 H, dd, *J* 8.1 and 5.4, 7-H^a), 4.05 (1 H, ddd, *J* 7.5, 6.3, and 5.4, 6-H), 4.13 (1 H, dd, *J* 8.1 and 6.3, 7-H^b), 4.37 (1 H, dd, *J* 7.5 and 1.5, 5-H), 4.95 (1 H, q, *J* 2.1, 4-H), 6.11 (1 H, dd, *J* 6.3 and 1.8, 2-H) and 7.27 (1 H, dd, *J* 6.3 and 2.1, 3-H); δ_C(75.4 MHz; $CDCl_3$) −4.9, −4.6, 17.9, 25.1, 25.6 (3 C), 26.5, 28.1 (3 C), 64.8, 68.0, 72.2, 77.4, 82.8, 109.8, 127.8, 147.5, 149.6 and 169.5.

2-(tert-*Butoxycarbonylamino*)-3-O-(tert-*butyldimethylsilyl*)-4,5-O-*isopropylidene*-D-*arabinose* **13a**.—The *title compound* was prepared from unsaturated lactam **12a** (2.5 g, 5.8 mmol) by following the procedure described for compound **5a**, and was obtained as an oil (1.4 g, 60%), $[\alpha]_D$ +25.0 (*c* 1.6, $CHCl_3$) (Found: C, 56.3; H, 9.2; N, 3.3. $C_{19}H_{37}NO_6Si$ requires C, 56.5; H, 9.2; N, 3.5%); δ_H(300 MHz; $CDCl_3$) 0.35 (3 H, s, Me), 0.62 (3 H, s, Me), 0.87 (9 H, s, Bu^t), 1.32 (3 H, s, Me), 1.41 (3 H, s, Me), 1.48 (9 H, s, Bu^t), 3.82 (1 H, m, 4-H), 3.9–4.1 (2 H, m, 5-H_2), 4.29 (1 H, dd, *J* 6.0 and 2.0, 3-H), 4.44 (1 H, dd, *J* 8.7 and 2.0, 2-H), 5.29 (1 H, d, *J* 8.7, NH) and 9.71 (1 H, s, 1-H); δ_C(75.4 MHz; $CDCl_3$) −4.5, −4.4, 18.0, 25.0, 25.7 (3 C), 26.5, 28.3 (3 C), 62.3, 66.2, 71.2, 76.5, 80.2, 109.3, 155.6 and 200.7.

The following amino aldehydes were obtained from the

corresponding lactam precursors by essentially the same procedure:

2-(tert-*Butoxycarbonylamino*)-3-O-(tert-*butyldimethylsilyl*)-2-*deoxy*-4,5-O-*isopropylidene*-L-*arabinose* **13b**. From lactam **12b** (2.0 g, 4.6 mmol), as an *oil* (1.1 g, 64%), $[\alpha]_D$ −24.3 (*c* 0.8, $CHCl_3$) (Found: C, 56.4; H, 9.3; N, 3.4%); ^1H and ^{13}C NMR, see compound **13a**.

2-(tert-*Butoxycarbonylamino*)-3-O-(tert-*butyldimethylsilyl*)-2-*deoxy*-4,5:6,7-*di*-O-*isopropylidene*-D-glycero-D-galacto-*heptose* **13c**. From lactam **12c** (1.5 g, 2.8 mmol), as an oil (0.86 g, 61%), $[\alpha]_D$ −6.9 (*c* 2.0, $CHCl_3$) (Found: C, 57.0; H, 9.2; N, 2.6. $C_{24}H_{45}NO_8Si$ requires C, 57.2; H, 9.0; N, 2.8%); δ_H(300 MHz; $CDCl_3$) 0.12 (3 H, s, Me), 0.16 (3 H, s, Me), 0.91 (9 H, s, Bu^t), 1.34 (6 H, s, 2 × Me), 1.36 (3 H, s, Me), 1.42 (3 H, s, Me), 1.46 (9 H, s, Bu^t), 3.81 (1 H, t, *J* 7.2, 5-H), 3.88 (1 H, dd, *J* 8.1 and 5.7, 7-H^a), 4.04 (2 H, m, 4- and 6-H), 4.12 (1 H, dd, *J* 8.1 and 6.0, 7-H^b), 4.25 (1 H, dd, *J* 5.7 and 3.0, 2-H), 4.55 (1 H, t, *J* 3.0, 3-H), 5.52 (1 H, d, *J* 5.7, NH) and 9.78 (1 H, s, 1-H); δ_C(75.4 MHz; $CDCl_3$) −4.8, −4.6, 18.0, 25.2, 25.8 (3 C), 26.6, 27.0, 27.1, 28.3 (3 C), 61.6, 67.5, 70.7, 77.2, 78.6, 80.0, 83.2, 109.7, 110.6, 155.7 and 200.8.

2-(tert-*Butoxycarbonylamino*)-3-O-(tert-*Butyldimethylsilyl*)-2-*deoxy*-4,5:6,7-*di*-O-*isopropylidene*-L-glycero-L-galacto-*heptose* **13d**. From lactam **12d** (1.0 g, 1.9 mmol), as an *oil* (0.63 g, 66%), $[\alpha]_D$ +6.0 (*c* 2.0, $CHCl_3$) (Found: C, 57.4; H, 9.2; N, 2.6%); ^1H and ^{13}C NMR, see compound **13c**.

6-O-*Benzyl*-2-(tert-*butoxycarbonylamino*)-3-O-(tert-*Butyldimethylsilyl*)-2-*deoxy*-4,5-O-*isopropylidene*-L-*galactose* **13e**. From lactam **12e** (1.5 g, 2.7 mmol), as an *oil* (0.86 g, 61%), $[\alpha]_D$ +18.9 (*c* 2.6, $CHCl_3$) (Found : C, 61.7; H, 8.4; N, 2.7. $C_{27}H_{45}NO_7Si$ requires C, 61.9; H, 8.7; N, 2.7%); δ_H(300 MHz; $CDCl_3$) 0.07 (3 H, s, Me), 0.09 (3 H, s, Me), 0.85 (9 H, s, Bu^t), 1.25 (3 H, s, Me), 1.38 (3 H, s, Me), 1.46 (9 H, s, Bu^t), 3.51 (1 H, dd, *J* 10.5 and 6.3, 6-H^a), 3.59 (1 H, dd, *J* 10.5 and 3.6, 6-H^b), 3.80 (1 H, t, *J* 7.2, 4-H), 4.13 (1 H, td, *J* 6.9 and 3.6, 5-H), 4.28 (2 H, m, 2-and 3-H), 4.56 (2 H, ABq, *J* 12.3, C*H*$_2$Ph), 5.39 (1 H, d, *J* 7.5, NH), 7.35 (5 H, m, CH_2*Ph*) and 9.75 (1 H, s, 1-H); δ_C(75.4 MHz; $CDCl_3$) −4.6, −4.5, 17.9, 25.7 (3 C), 25.9, 27.1, 28.3 (3 C), 62.5, 71.3, 71.9, 73.5, 78.6, 78.9, 80.1, 110.2, 127.7 (2 C), 127.8, 128.3 (2 C), 137.7, 155.6 and 200.6.

2-(tert-*Butoxycarbonylamino*)-3-O-(tert-*butyldimethylsilyl*)-2-*deoxy*-4,5-O-*isopropylidene*-D-*ribose* **13f**. From lactam **12f** (1.2 g, 2.8 mmol), as an *oil* (0.68 g, 60%), $[\alpha]_D$ −17.5 (*c* 0.6, $CHCl_3$) (Found: C, 56.3; H, 9.0; N, 3.3. $C_{19}H_{37}NO_6Si$ requires C, 56.5; H, 9.2; N, 3.5%); δ_H(300 MHz; $CDCl_3$) 0.08 (3 H, s, Me), 0.10 (3 H, s, Me), 0.85 (9 H, s, Bu^t), 1.35 (3 H, s, Me), 1.43 (3 H, s, Me), 1.45 (9 H, s, Bu^t), 3.90 (1 H, m, 4-H), 4.1–4.2 (3 H, m, 3-H and 5-H_2), 4.54 (1 H, br d, *J* 6.0, 2-H), 5.37 (1 H, d, *J* 6.0, NH) and 9.71 (1 H, s, 1-H); δ_C(75.4 MHz; $CDCl_3$) −4.8, −4.6, 17.9, 25.0, 25.6 (3 C), 26.3, 28.3 (3 C), 63.0, 67.7, 75.0, 76.3, 79.9, 110.1, 154.9 and 198.3.

2-*Amino*-2-*deoxy*-D-*arabinonic Acid* (4-epi-*Polyoxamic Acid*) **14a**.—The title compound was prepared by starting with the aldehyde **13a** (1.0 g, 2.5 mmol), following sequentially the procedures described for compounds **6a** and **7a**; compound **14a** was obtained as a foam (0.31 g, 76%), $[\alpha]_D$ +5.0 (*c* 0.2, water); δ_H(300 MHz; CD_3OD + TFA) 3.77 (1 H, dd, *J* 13.2 and 2.7, 5-H^b), 4.01 (1 H, dd, *J* 13.2 and 2.1, 5-H^a), 4.40 (1 H, d, *J* 8.0, 2-H), 4.44 (1 H, ddd, *J* 6.6, 2.7, and 2.1, 4-H) and 4.76 (1 H, dd, *J* 8.0 and 6.6, 3-H); δ_C(75.4 MHz; D_2O + CD_3OD) 55.5, 63.3, 70.1, 72.8 and 171.8; (Found: $[M + H]^+$, 166.0719. $C_5H_{12}NO_5$ requires *m*/*z*, 166.0715).

N-(*tert*-Butoxycarbonyl)-3-*O*-(*tert*-butyldimethylsilyl)-4,5-*O*-isopropylidene-protected intermediate: $[\alpha]_D$ +25.0 (*c* 1.6, $CHCl_3$); δ_H(300 MHz; $CDCl_3$) 0.06 (3 H, s, Me), 0.12 (3 H, s, Me), 0.87 (9 H, s, Bu^t), 1.33 (3 H, s, Me), 1.43 (3 H, s, Me), 1.46 (9 H, s, Bu^t), 3.85 (1 H, dd, *J* 8.0 and 6.0, 5-H^a), 3.96 (1 H, t, *J* 8.0, 5-H^b), 4.05 (1 H, t, *J* 6.3, 4-H), 4.32 (1 H, br d, *J* 5.4, 3-H), 4.56 (1 H, br d, *J* 9.0, 2-H), and 5.18 (1 H, br d, *J* 9.0, NH); δ_C(75.4 MHz; $CDCl_3$) −4.5 (2 C), 18.1, 25.2, 25.8 (3 C), 26.7, 28.3 (3 C), 55.8, 65.9, 72.8, 76.4, 80.4, 109.1, 155.9 and 175.2.

The following amino acids were obtained from the respective aldehyde precursors by essentially the same procedure:

2-*Amino*-2-*deoxy*-L-*arabinoic acid* (2,3-*di*-epi-*polyoxamic acid*) **14b**. Obtained in 81% yield as a *foam*, $[\alpha]_D$ −4.8 (*c* 0.1, water); ^1H and ^{13}C NMR, see compound **14a** (Found: $[M + H]^+$, 166.0711).

2-*Amino*-2-*deoxy*-D-glycero-D-galacto-*heptonic acid* **14c**. Obtained in 84% yield as a *foam*, $[\alpha]_D$ −16 (*c* 0.2, water); δ_H(300 MHz; D_2O + CD_3OD) 3.6–3.8 (3 H, m), 3.8–3.9 (2 H, m), 4.05 (1 H, d, *J* 1.8) and 4.23 (1 H, dd, *J* 8.1 and 1.8); δ_C(75.4 MHz; D_2O + CD_3OD) 57.1, 64.1, 69.8, 70.2, 70.7, 71.9 and 174.2; (Found: $[M + H]^+$, 226.0930. $C_7H_{16}NO_7$ requires *m*/*z*, 226.0927).

N-(*tert*-Butoxycarbonyl)-3-*O*-(*tert*-butyldimethylsilyl)-4,5:6,7-di-*O*-isopropylidene-protected intermediate: $[\alpha]_{365}$ +6.0 (*c* 1.0, $CHCl_3$); δ_H(300 MHz; $CDCl_3$) 0.14 (3 H, s, Me), 0.18 (3 H, s, Me), 0.92 (9 H, s, Bu^t), 1.34 (3 H, s, Me), 1.36 (3 H, s, Me), 1.40 (3 H, s, Me), 1.41 (3 H, s, Me), 1.46 (9 H, s, Bu^t), 3.89 (1 H, dd, *J* 8.0 and 5.7, 7-H^a), 3.90 (1 H, m), 4.05 (2 H, m), 4.13 (1 H, dd, *J* 8.0 and 6.0, 7-H^b), 4.46 (1 H, dd, *J* 7.5 and 2.7), 4.53 (1 H, br s) and 5.43 (1 H, br d, *J* 6.9, NH); δ_C(75.4 MHz; $CDCl_3$) −4.9, −4.6, 17.9, 25.2, 25.8 (4 C), 26.5, 27.3, 28.3 (3 C), 54.5, 67.5, 71.5, 78.9 (2 C), 80.4, 82.4, 109.8, 110.6, 155.9 and 173.8.

2-*Amino*-2-*deoxy*-L-glycero-L-galacto-*heptonic acid* **14d**. Obtained in 79% yield as a *foam*; $[\alpha]_D$ +16.4 (*c* 0.24, water); ^1H and ^{13}C NMR, see compound **14c** (Found: $[M + H]^+$, 226.0921).

2-*Amino*-2-*deoxy*-D-*ribonic acid* (2,4-*di*-epi-*polyoxamic acid*) **14f**. Obtained as a foam in 80% yield, $[\alpha]_{365}$ −2.7 (*c* 0.2, water); δ_H(300 MHz; CD_3OD + TFA) 3.80 (1 H, dd, *J* 12.5 and 3.3, 5-H^b), 3.86 (1 H, dd, *J* 12.5 and 3.0, 5-H^a), 4.41 (1 H, dt, *J* 3.3 and 3.0, 4-H), 4.50 (1 H, d, *J* 5.7, 2-H) and 4.82 (1 H, d, *J* 5.7, 3-H); δ_C(75.4 MHz; D_2O) 55.0, 60.9, 68.2, 70.3 and 172.5 (Found: $[M + H]^+$, 166.0711. $C_5H_{12}NO_5$ requires *m*/*z*, 166.0715).

N-(*tert*-Butoxycarbonyl)-3-*O*-(*tert*-butyldimethylsilyl)-4,5-*O*-isopropylidene-protected intermediate: $[\alpha]_D$ −48.0 (*c* 0.5, $CHCl_3$); δ_H(300 MHz; $CDCl_3$) 0.09 (3 H, s, Me), 0.13 (3 H, s, Me), 0.86 (9 H, s, Bu^t), 1.36 (3 H, s, Me), 1.45 (9 H, s, Bu^t), 1.46 (3 H, s, Me), 4.03 (1 H, m), 4.13 (2 H, m), 4.17 (1 H, ddd, *J* 12.0, 6.3, and 6.1), 4.56 (1 H, br d, *J* 7.0, 2-H) and 5.43 (1 H, d, *J* 7.0, NH); δ_C(75.4 MHz; $CDCl_3$) −4.8, −4.6, 17.9, 24.7, 25.6 (3 C), 25.9, 28.3 (3 C), 56.7, 66.8, 74.6, 77.0, 79.9, 110.2, 155.1 and 172.6.

2-*Amino*-2-*deoxy*-L-*galactonic Acid* **14e**.—Protected aldehyde **13e** (0.6 g, 1.13 mmol) was oxidized by essentially the same procedure as for the preparation of compound **6a** to give 6-*O*-benzoyl-2-(*tert*-butoxycarbonylamino)-3-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-4,5-*O*-isopropylidene-L-galactonic acid intermediate as an oil, δ_H(300 MHz; $CDCl_3$) 0.09 (3 H, s, Me), 0.13 (3 H, s, Me), 0.88 (9 H, s, Bu^t), 1.43 (3 H, s, Me), 1.45 (3 H, s, Me), 1.46 (9 H, s, Bu^t), 3.99 (1 H, br t, *J* 7.2), 4.37 (3 H, m), 4.48 (1 H, m), 4.62 (1 H, br d, *J* 9.0, 2-H), 5.27 (1 H, d, *J* 9.0, NH), 7.44 (2 H, t, *J* 7.8, H_{meta}), 7.57 (1 H, tt, *J* 7.5 and 1.5, H_{para}) and 8.07 (2 H, dd, *J* 6.9 and 1.5, H_{ortho}); δ_C(75.4 MHz; $CDCl_3$) −4.6, −4.3, 18.0, 25.8 (3 C), 27.2, 27.5, 28.2 (3 C), 55.7, 65.8, 73.3, 78.1, 80.5, 81.9, 110.6, 128.4 (2 C), 128.5, 129.7 (2 C), 133.1, 156.0, 166.2 and 175.3.

A mixture of the above protected intermediate and NaOMe (20 mg) in methanol (2 cm^3) was stirred at room temperature for 30 min. The solution was then acidified with TFA (2 cm^3) and the mixture was stirred for an additional 1 h. The solvent was evaporated off and the residue was subjected to flash chromatographic purification on silica gel and eluted with 6:4:1 CH_2Cl_2–MeOH–30% aq. NH_4OH. Removal of the

solvent and lyophilization furnished pure *amino acid* **14e** (0.19 g, 74% from **13e**) as a foam, $[\alpha]_D$ + 10.2 (*c* 0.2, water); δ_H(300 MHz; CD_3OD + TFA) 4.22 (1 H, m), 4.39 (1 H, m), 4.4–4.5 (2 H, m), 4.85 (1 H, m) and 4.67 (1 H, br s); δ_C(75.4 MHz; CD_3OD + TFA) 57.1, 66.3, 69.6, 73.9, 77.7 and 170.2 (Found: $[M + H]^+$, 196.0817. $C_6H_{14}NO_6$ requires *m/z* 196.0821).

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