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Divergent Synthesis of 3-Amino-3-deoxy- and 4-Amino-4-deoxyhexoses

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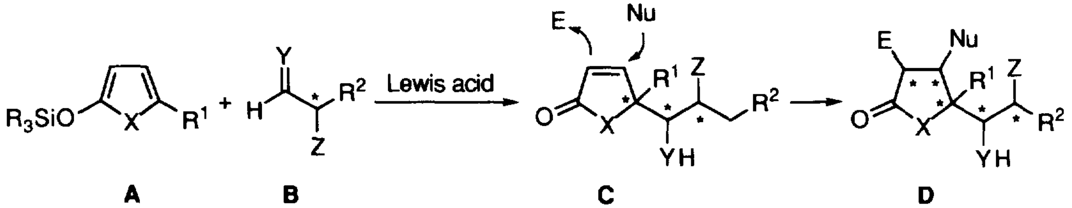
Abstract: A new efficient synthesis of 3-amino-3-deoxy-D-altrose (**13**), 3-amino-3-deoxy-L-allose (**17**), and 4-amino-4-deoxy-D-talose (**21**) from 2,3-*O*-isopropylidene-D-glyceraldehyde (**6**) using *N*-(*tert*-butoxycarbonyl)-2-(*tert*-butyldimethylsiloxy)pyrrole (TBSOP) as homologative nucleophile is described. The procedure highlights the merits of densely functionalized homochiral heptonolactam **9** as a key divergent intermediate.

There has been continuing interest in the development of new methods to access enantiomerically pure carbohydrates including thio- and aminosugars.[1] Those approaches which exploit readily available homochiral sources, for example, by using carbohydrate-derived frames or amino acids are especially attractive.[1,2] Recent work of our laboratory[3] has established that Lewis acid-assisted elongation of α-chiral aldehyde or imine precursors of type **B** with oxygen, sulphur, and nitrogen siloxydienes **A** (X = O, S, NBoc) generates unsaturated intermediates **C**, which can function as templates to forge the skeletons of a number of densely functionalized compounds (*e.g.* **D**) equipped with diverse substitution and chirality (Scheme 1).

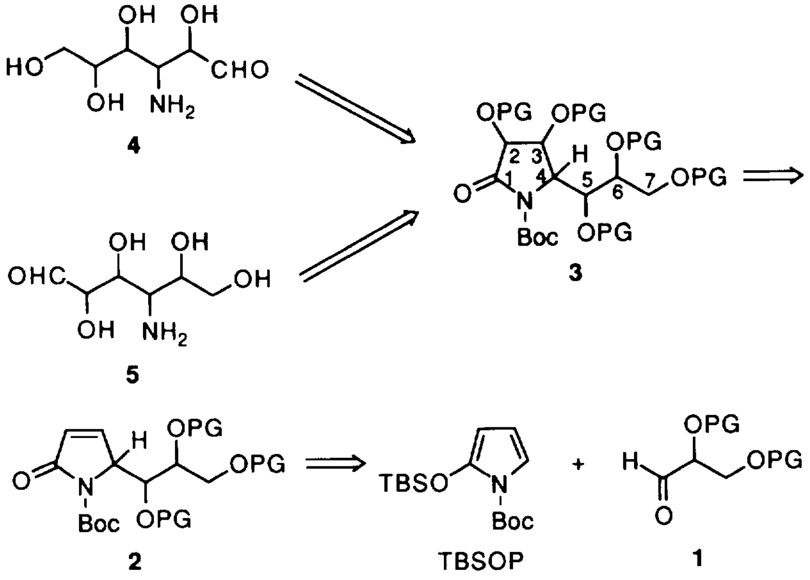
Scheme 1



As a further exploitation of this synthetic tactic, we wish now to report on the use of *N*-(*tert*-butoxycarbonyl)-2-(*tert*-butyldimethylsiloxy)pyrrole (hereafter TBSOP) to assemble rare amino sugars,[4] including 3-amino-3-deoxy-D-altrose (**13**), 3-amino-3-deoxy-L-allose (**17**), and 4-amino-4-deoxy-D-talose (**21**).

Planning. A retrosynthetic analysis of open-chain 3-amino- and 4-aminohexoses of general formulas **4** and **5**, based on TBSOP-involving chemistry, is outlined in Scheme 2. This strategy relies on the rapid construction of the seven-carbon aminated matrices **2** by coupling of TBSOP to protected glyceraldehyde **1**, followed by the introduction of two OH-groups at C(2) and C(3) by dihydroxylation of the lone double-bond within **2** to generate **3**.

Scheme 2



PG = Protective groups

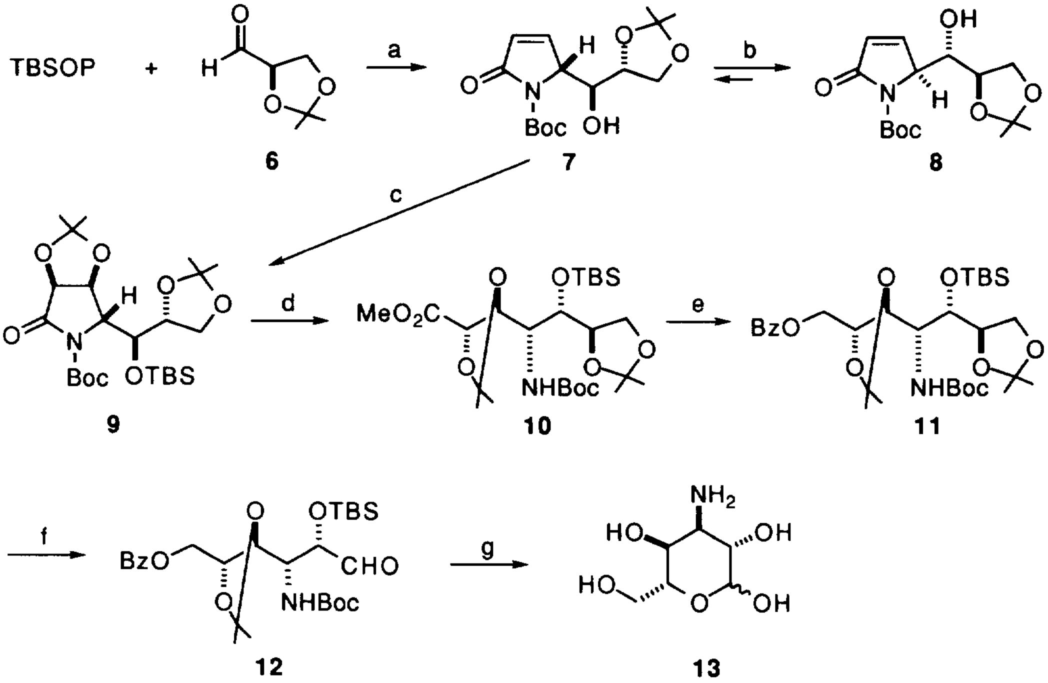
For 3-aminohexoses **4**, we choose to first reduce the C(1) carbonyl of **3** to CH_2OH, and then create the aldehyde function on C(6) by oxidative fragmentation of the C(6)-C(7) diol, while for 4-amino-derivatives **5** we plan to first generate the terminal CH_2OH on C(6) by excision of the terminal carbon atom, and then implement the aldehyde group on C(1) by reduction of the γ-lactone function. Since lactones **2** can be available, in enantiomerically pure forms, with either 4,5-*threo* or 4,5-*erythro* configuration employing homochiral glyceraldehyde synthons,[5] access to diverse stereochemical variants of **4** and **5** would be secured.

Synthesis of 3-Aminohexoses. To access diastereomeric aminosugars **13** and **17**, the entire plan outlined in Schemes 3 and 4 was executed, with parallel chemistry, utilizing the C-4 epimeric templates **7** and **8**. As described earlier,[5] crystalline lactam **7** was easily accessible by $SnCl_4$-catalyzed addition of TBSOP to 2,3-*O*-isopropylidene-D-glyceraldehyde (**6**) in 80% isolated yield, whereas the alternative matrix **8** was conveniently obtained from **7** by base-promoted C(4) epimerization (Et_3N, DMAP) in 64% yield.

The preparation of D-altrose derivative **13** called for 4,5-*threo*-5,6-*erythro* configured heptenonolactam **7** as the requisite precursor. As depicted in Scheme 3, after protection of the free OH-group within **7** as TBS-ether, selective anti-cis dihydroxylation of the lone double bond was accomplished by exposing the unsaturated lactam to $KMnO_4$/dicyclohexano-18-crown-6 ether to furnish a single diol intermediate (not shown), which was then subjected to conventional acetonidation (2,2-dimethoxypropane, TsOH) to afford the highly functionalized lactam **9** in a good 38% overall yield from **7**. Remarkably, facial selectivity was complete, and relative stereocontrol provided by the C(4) stereocenter of **7** led to addition anti to the triol side-chain.

The structural assignment of **9** was fairly straightforward. In the proton NMR spectrum of this compound two one-proton doublets at δ 4.75 and δ 4.66 ($J_{2,3}$ = 5.5 Hz) were assigned to the cis-oriented ring junction protons H(2) and H(3), respectively, while a one-proton doublet at δ 4.21 ($J_{3,4}$ = 0.0 Hz; $J_{4,5}$ = 3.5 Hz) was assigned to trans-disposed H(4). The relative stereochemistry shown was also corroborated by NOESY experiments displaying an intense interaction between H(2) and H(3), which are located on the same side of the ring, but not between H(3) and H(4), suggesting they are trans to each other.

Scheme 3



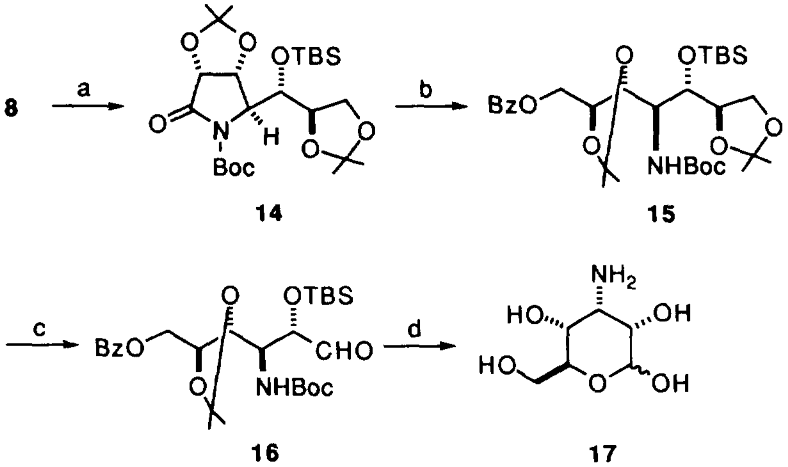
(a) $SnCl_4$, Et_2O, -80°C. (b) Et_3N, DMAP, CH_2Cl_2, rt. (c) 1. TBSCl, DMF, imidazole; 2. $KMnO_4$, DCH-18-crown-6 ether, CH_2Cl_2; 3. DMP, TsOH. (d) 1M aq LiOH, THF; 2. CH_2N_2, Et_2O. (e) 1. $NaBH_4$, $(C_{18}H_{17})_3N^+CH_3Cl^-$, C_6H_6/H_2O, reflux; 2. BzCl, DMAP, pyridine, rt. (f) 1. 70% aq AcOH, 50°C; 2. 0.65 M aq $NaIO_4$, SiO_2, CH_2Cl_2. (g) 1. 3N HCl, THF; 2. MeOH, MeONa, rt.

The next task was to transform the C(1) lactam carbonyl of **9** into the terminal CH_2OH of the target aminosugar **13**; and this was performed by a four-step protocol comprising hydrolytic ring opening (LiOH, THF) and methyl ester formation (CH_2N_2) to give the open-chain γ-amino ester **10**, followed by ester-to-carbinol reduction ($NaBH_4$, aliquat) and benzoylation of the hydroxymethyl function so formed. In the event, fully protected aminoheptitol **11** was obtained in 31% yield from **9**.

In the final stages of the sequence, the isopropylidene protection at the right-hand terminus of the chain of **11** was selectively cleaved by acidic treatment (AcOH), and the resulting diol was oxidatively shortened by one carbon ($NaIO_4$) to generate the differently protected aldehydo-hexose **12** in 64% yield from **11**. Removal of all the acid-sensitive protective groups of **12** by aqueous HCl in THF, followed by MeONa-catalyzed debenzoylation, finally furnished 3-amino-3-deoxy-D-altrose **13**, here depicted in its pyranose form, in almost quantitative yield.

The above synthetic sequence to **13** was then paralleled to create the L-allose derivative **17**, utilizing the chiral framework of the unsaturated lactam **8** (Scheme 4).

Scheme 4



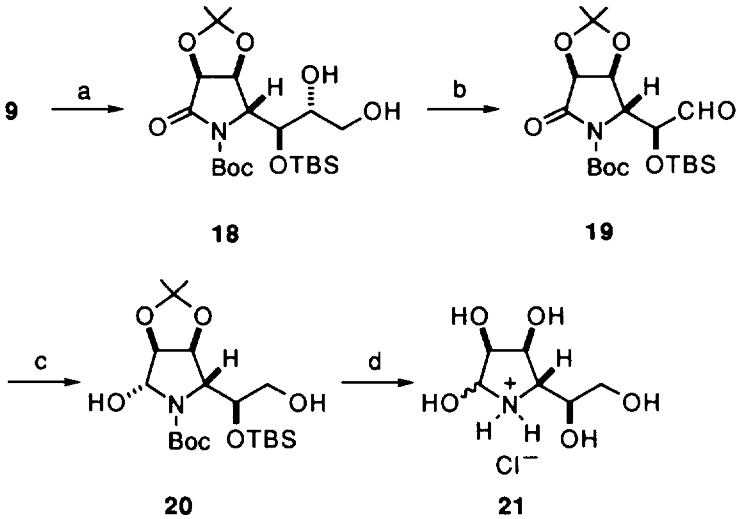
(a) 1. TBSCl, DMF, imidazole; 2. $KMnO_4$, DCH-18-crown-6 ether, CH_2Cl_2; 3. DMP, TsOH. (b) 1M aq LiOH, THF; 2. CH_2N_2, Et_2O; 3. $NaBH_4$, $(C_{18}H_{17})_3N^+CH_3Cl^-$, C_6H_6/H_2O, reflux; 4. BzCl, DMAP, pyridine, rt. (c) 1. 70% aq AcOH, 50°C; 2. 0.65 M aq $NaIO_4$, SiO_2, CH_2Cl_2. (d) 1. 3N HCl, THF; 2. MeOH, MeONa, rt.

Thus, fully functionalized heptonolactam **14** was prepared from **8** via double-bond dihydroxylation and protective work-up by the same set of reactions as described for compound **9** (33% yield from **8**); and this material was rapidly elaborated into the open-chain heptitol **15** utilizing the clean procedure previously adopted to convert **9** into **11**. In our hand, the four-reaction sequence (*i.e.* ring opening, methyl ester formation, $NaBH_4$ reduction, and benzoylation) allowed **15** to be formed with an acceptable 29% overall yield. Finally, the formyl carbon was derived by oxidative sacrifice of the terminal carbon atom within **15** to furnish the aminoaldose **16** (65%), whose structure was quickly ascertained by ^1H and ^{13}C NMR experiments. Sequential acidic and basic treatments (HCl, then MeONa) liberated 3-amino-3-deoxy-L-allose **17**, which was recovered as lyophilized free-base powder in 90% yield.

Synthesis of 4-Amino-4-deoxy-D-talose. The synthesis of the title candidate **21** commenced with enantiopure heptonolactam **9**, the same source with which 3-aminosugar **13** was previously created. As depicted in Scheme 5, the key operation simply involved one-carbon shortening at the right-side of **9**, followed by creation of the "anomeric" carbon at C(1). Thus, lactam **9** was sequentially exposed to aqueous acetic acid to remove the terminal acetonide protection to form **18** (68%), and then to $NaIO_4$ to cleave the vicinal diol function to create the aldehydo-lactam **19**, which was recovered in 95% yield and used as such in the subsequent stages of the synthesis. Fortunately enough, treatment of **19** with $NaBH_4$ in methanol ensured the reduction of the aldehyde function to CH_2OH, as expected, accompanied by concomitant and highly selective transformation of the lactam carbonyl into the requisite anomeric aminol group. Thus, in a sole operation, partially protected 4-aminohexose **20** was produced in 78% isolated yield. Accurate NMR analyses, including COSY and NOESY experiments, firmly established the β-pyrrolidinose nature of the sugar, as well as the exact stereodisposition of the five consecutive chiral centers.[6]

Remarkably, the final acidic deprotective work-up (3N HCl in THF) furnished the pentahydroxylated pyrrolidine **21**, quantitatively, which was recovered as its hydrochloride salt, as a 6:4 mixture of α and β anomers.

Scheme 5



(a) 70% aq AcOH, 40°C. (b) 0.65M aq $NaIO_4$, SiO_2, CH_2Cl_2. (c) $NaBH_4$, MeOH, -20°C to 0°C. (d) 3N, HCl, THF.

Conclusion. In summary, this process for assembling diverse aminated hexoses, **13** and **17**, in a diastereoselective sense, by starting with TBSOP and readily available chiral sources, and the synthesis of densely oxygenated homochiral pyrrolidinose **21** has been shown to be highly efficient. According to a divergent plan, by exploiting a common precursor, **9**, and adopting complementary bilateral manipulations at the left and the right side of the molecule, access to either 3-aminohexopyranose **13** or pyrrolidinose **21** was secured. The results herein, emphasizing the power of TBSOP in asymmetric synthesis, pave the way for future application of this technique to access many variants of oxygen- and nitrogen-containing chiral carbohydrate-like molecules.

EXPERIMENTAL

General. The ^1H and ^{13}C NMR spectra were recorded on a Varian VXR-300 and on a Bruker AC-300 instruments operating at 300.0 MHz and 75.4 MHz, respectively. Chemical shifts are related to tetramethylsilane. Optical rotations ($[\alpha]_D$) were measured on a Perkin-Elmer 241 instrument and are recorded in units of 10^{-1} deg cm^2 g^{-1}. Column chromatography was invariably performed on Merck silica gel 70-230 Mesh.

Kieselgel 60 F_{254} (from Merck) was used for TLC. Elemental analyses were performed by Microanalytical Laboratory of University of Sassari.

The preparation of *N*-(*tert*-butoxycarbonyl)-2-(*tert*-butyldimethylsiloxy)pyrrole (TBSOP) was carried out by the method in our precedent papers.[5] 2,3-*O*-Isopropylidene-D-glyceraldehyde (**6**) was prepared from 1,2:5,6-di-*O*-isopropylidene-D-mannitol (Fluka) by periodate fission and used immediately.[7]

***N*-(*tert*-Butoxycarbonyl)-6,7-*O*-isopropylidene-2,3-dideoxy-D-*arabino*-hept-2-enono-1,4-lactam (7).** This material was prepared from TBSOP and **6** according to a previously reported procedure.[5] Significant data: mp 138-140°C; $[\alpha]^{20}_D$ +197.6° (*c* 0.8, $CHCl_3$); δ_H (300 MHz, $CDCl_3$) 7.43 (dd, 1H, *J* = 6.3, 2.1 Hz), 6.13 (dd, 1H, *J* = 6.3, 1.5 Hz), 4.81 (dt, 1H, *J* = 5.7, 2.4 Hz), 4.09 (ddd, 1H, *J* = 6.0, 5.7, 3.9 Hz), 4.01 (q, 1H, *J* = 6.0 Hz), 3.94 (dd, 1H, *J* = 8.1, 6.0 Hz), 3.86 (dd, 1H, *J* = 8.1, 6.0 Hz), 3.63 (d, 1H, *J* = 3.9 Hz), 1.57 (s, 9H), 1.37 and 1.32 (2s, each 3H); δ_C (75.4 MHz, $CDCl_3$) 168.9, 150.9, 148.2, 126.9, 109.2, 83.8, 75.6, 72.6, 66.4, 65.6, 28.0, 26.4, 25.1.

***N*-(*tert*-Butoxycarbonyl)-6,7-*O*-isopropylidene-2,3-dideoxy-D-*ribo*-hept-2-enono-1,4-lactam (8).** This material was prepared from TBSOP and **6** according to a previously reported procedure.[5] Significant data: mp 120-122°C; $[\alpha]^{20}_D$ -120.0° (*c* 1.1, $CHCl_3$); δ_H (300 MHz, $CDCl_3$) 7.29 (dd, 1H, *J* = 6.3, 2.1 Hz), 6.16 (dd, 1H, *J* = 6.3, 2.0 Hz), 4.97 (q, 1H, *J* = 2.1 Hz), 4.20 (m, 1H), 4.15 (td, 1H, *J* = 6.6, 2.2 Hz), 4.03 (m, 2H), 3.49 (d, 1H, *J* = 6.6 Hz), 1.56 (s, 9H), 1.46 and 1.37 (2s, each 3H); δ_C (75.4 MHz, $CDCl_3$) 170.0, 149.7, 147.2, 128.0, 109.9, 83.5, 76.3, 71.4, 67.9, 65.1, 28.1, 26.7, 24.5.

***N*-(*tert*-Butoxycarbonyl)-2,3:6,7-di-*O*-isopropylidene-5-*O*-(*tert*-butyldimethylsilyl)-D-*glycero*-D-*talo*-heptono-1,4-lactam (9).** To a solution of **7** (1.2 g, 3.83 mmol) in anhydrous DMF (12 mL) imidazole (2.64 g, 38.30 mmol) and TBSCl (5.94 g, 38.30 mmol) were added. The reaction mixture was stirred under argon for 12 h and then 5% aq citric acid solution (10 mL) was added. The mixture was extracted with AcOEt (3x30 mL) and dried with $MgSO_4$. The solution was evaporated under reduced pressure and the crude product was purified by flash chromatography (9:1 CH_2Cl_2/diethyl ether) to afford 1.28 g of the expected compound. To 1.28 g (2.99 mmol) of this product dissolved in CH_2Cl_2 (20 mL), $KMnO_4$ (572 mg, 3.59 mmol) and *cis*-dicyclohexano-18-crown-6 ether (46 mg, 0.12 mmol) were added. The reaction mixture was stirred for 2 h, then a saturated Na_2SO_3 aqueous solution was added. After neutralization with a saturated aqueous citric acid solution the mixture was extracted with CH_2Cl_2 (3x30 mL) and AcOEt (3x30 mL). The collected organic extracts was dried with $MgSO_4$ and evaporated under reduced pressure. The crude product was dissolved in DMP (15 mL) and TsOH (22 mg) was added. The reaction mixture was stirred for 1 h then a saturated $NaHCO_3$ aqueous solution was added. The mixture was extracted with CH_2Cl_2 (3x10 mL), the extracts were dried with $MgSO_4$ and then evaporated under reduced pressure. The resulting crude product was purified by flash chromatography (7:3 hexanes/ethyl acetate) to afford **9** (730 mg, 1.45 mmol) as a white solid in 38% yield from **7**: mp 94-96°C; (Found: C, 57.41; H, 8.59; N, 2.85. $C_{24}H_{43}NO_8Si$ requires C, 57.46; H, 8.64; N, 2.79%); $[\alpha]^{20}_D$ +32.3° (*c* 4.0, $CHCl_3$); δ_H (300 MHz, $CDCl_3$) 4.75 (d, 1H, *J* = 5.5 Hz), 4.66 (d, 1H, *J* = 5.5 Hz), 4.21 (d, 1H, *J* = 3.5 Hz), 4.10 (m, 2H), 3.83 (m, 1H), 3.72 (dd, 1H, *J* = 8.1, 5.7 Hz), 1.54 (s, 9H), 1.45 and 1.38 (2s, each 3H), 1.29 and 1.27 (2s, each 3H), 0.91 (s, 9H), 0.23 and 0.15 (2s, each

3H); δ_C (75.4 MHz, CDCl$_3$) 170.6, 150.0, 111.7, 110.2, 83.0, 77.6, 76.0, 71.8, 69.8, 68.9, 63.2, 28.0, 26.9, 26.1, 25.4, 24.9, 17.6, -4.2, -5.1.

Methyl 2,3:6,7-Di-*O*-isopropylidene-4-[*N*-(*tert*-butoxycarbonylamino)]-5-*O*-(*tert*-butyldimethylsilyl)-4-deoxy-D-*glycero*-D-*talo*-heptonate (10). To a solution of **9** (496 mg, 0.99 mmol) in THF (8 mL) a 1M aqueous LiOH solution (5 mL) was added dropwise. The mixture was stirred for 3 h and then extracted with AcOEt (3x10 mL). After drying (MgSO$_4$), the organic layer was evaporated under reduced pressure. The residue obtained was dissolved in Et$_2$O (10 mL) and then an ethereal solution of diazomethane was added until appearance of a yellow colouring. The solvent was evaporated under reduced pressure to give a crude product that was purified by flash chromatography (8:2 hexanes/ethyl acetate) to afford **10** (396 mg, 75%) as a glass; (Found: C, 56.31; H, 8.83; N, 2.58. $C_{25}H_{47}NO_9Si$ requires C, 56.26; H, 8.88; N, 2.62%); $[\alpha]^{20}_D$ +27.8° (*c* 0.7, CHCl$_3$); δ_H (300 MHz, CDCl$_3$) 4.53-4.59 (m, 2H), 4.45 (dd, 1H, *J* = 10.5, 6.6 Hz), 4.13 (t, 1H, *J* = 6.6 Hz), 4.03 (dd, 1H, *J* = 7.8, 6.6 Hz), 3.95-3.99 (m, 1H), 3.83 (dd, 1H, *J* = 7.8, 6.6 Hz), 3.71 and 1.60 (2s, each 3H), 1.42 (s, 9H), 1.40 and 1.32 (2s, each 3H), 0.87 (s, 9H), 0.14 and 0.92 (2s, each 3H); δ_C (75.4 MHz, CDCl$_3$) 170.2, 154.3, 111.2, 108.8, 79.2, 77.2, 76.6, 73.8, 67.0, 54.6, 52.4, 28.3, 26.7, 26.4, 25.8, 25.6, 24.8, 17.9, -4.61.

1-*O*-Benzoyl-2,3:6,7-di-*O*-isopropylidene-4-[*N*-(*tert*-butoxycarbonylamino)]-5-*O*-(*tert*-butyldimethylsilyl)-4-deoxy-D-*glycero*-D-*talo*-heptitol (11). To a solution of **10** (276 mg, 0.52 mmol) in benzene (20 mL) and H$_2$O (15 mL) $(C_{18}H_{17})_3N^+CH_3Cl^-$ (aliquat, 10 mg) and NaBH$_4$ (100 mg, 2.64 mmol) were added. The solution was heated under reflux for 12 h, the organic phase was separated and aqueous layer was extracted with AcOEt (3x10 mL). The combined organic extracts were dried with MgSO$_4$ and evaporated under reduced pressure to give a crude product that was purified by flash chromatography (8:2 hexanes/ethyl acetate) to afford 139 mg of the reduced compound. This product (0.27 mmol) was dissolved in pyridine (2 mL), then BzCl (33 µL, 0.28 mmol) and DMAP (10 mg) were added under argon. The mixture was stirred at room temperature for 2h, H$_2$O was added and then the solution was extracted with AcOEt (3x10 mL). The combined organic extracts were dried with MgSO$_4$ and evaporated under reduced pressure. The crude product was purified by flash chromatography (9:1 hexanes/ethyl acetate) to afford **11** (129 mg, 41%) as an oil; (Found: C, 61.10; H, 8.50; N, 2.27. $C_{31}H_{51}NO_9Si$ requires C, 61.06; H, 8.43; N, 2.30%); $[\alpha]^{20}_D$ +46.4° (*c* 0.8, CHCl$_3$); δ_H (300 MHz, CDCl$_3$) 8.22-8.41 (m, 2H), 7.52-7.58 (m, 1H), 7.41-7.48 (m, 2H), 4.76 (dd, 1H, *J* = 11.0, 2.4 Hz), 4.75 (s, 1H), 4.46-4.50 (m, 1H), 4.42 (dd, 1H, *J* = 11.0, 7.2 Hz), 4.35 (d, 1H, *J* = 4.5 Hz), 3.99-4.06 (m, 3H), 3.79-3.91 (m, 2H), 1.46 (s, 6H), 1.43 (s, 9H), 1.30 (s, 3H), 0.93 (s, 9H), 0.17 and 0.15 (2s, each 3H); δ_C (75.4 MHz, CDCl$_3$) 166.0, 155.0, 132.8, 129.7, 128.2, 109.1, 108.1, 80.1, 77.2, 75.8, 75.2, 70.9, 64.8, 63.2, 51.1, 28.2, 27.9, 26.3, 26.1, 25.9, 24.8, 18.3, -3.8, -4.4.

2-*O*-(*tert*-Butyldimethylsilyl)-3-[*N*-(*tert*-butoxycarbonylamino)]-4,5-*O*-isopropylidene-6-*O*-benzoyl-3-deoxy-D-altrose (12). Compound **11** (100 mg, 0.16 mmol) was dissolved in 3 mL of 70% aq AcOH and the mixture was heated to 50-60°C for 12 h until complete disappearance of the starting material (TLC, 6:4 hexanes/ethyl acetate). A saturated aqueous NaHCO$_3$ solution (3 mL) was added and then the solution was extracted with AcOEt (3x10 mL). The combined organic extracts were evaporated under reduced pressure and the crude product obtained was purified by flash chromatography (6:4 hexanes/ethyl acetate) to afford 71 mg of a pure product. To a solution of 71 mg of this compound (0.12 mmol) in CH$_2$Cl$_2$

(4mL), SiO_2 (190 mg) and 0.65 M aqueous $NaIO_4$ solution (0.25 mL, 0.16 mmol) were added under stirring. The suspension was stirred for 3 h, then filtered. The organic layers were dried with $MgSO_4$ and evaporated under reduced pressure to give **12** (56 mg, 64%) as a glass; (Found: C, 60.27; H, 8.11; N, 2.55. $C_{27}H_{43}NO_8Si$ requires C, 60.31; H, 8.06; N, 2.60%); $[\alpha]^{20}_D$ +69.6° (*c* 1.9, $CHCl_3$); δ_H (300 MHz, $CDCl_3$) 9.60 (s, 1H), 8.06-8.09 (m, 2H), 7.54-7.57 (m, 1H), 7.42-7.47 (m, 2H), 4.78 (d, 1H, *J* = 10.5 Hz), 4.69 (bd, 1H, *J* = 10.5 Hz), 4.59 (bs, 1H), 4.49 (m, 1H), 4.36-4.42 (m, 2H), 4.17 (dd, 1H, *J* = 10.5, 6.0 Hz), 1.49 (s, 3H), 1.37 (s, 9H), 1.36 (s, 3H), 0.96 (s, 9H), 0.14 and 0.08 (2s, each 3H); δ_C (75.4 MHz, $CDCl_3$) 199.9, 166.2, 154.9, 134.4, 132.9, 129.7, 128.3, 109.3, 80.6, 78.1, 75.5, 74.3, 63.2, 49.9, 28.1, 28.0, 25.8, 25.6, 18.3, -4.4, -5.3.

3-Amino-3-deoxy-D-altrose (13).[8] To a solution of **12** (40 mg, 0.07 mmol) in THF (2mL), a 6N HCl solution in THF (3 mL, 1:1 v/v) was added. The mixture was stirred for 3 h, then the solvent was evaporated under reduced pressure. The crude product was dissolved in MeOH and treated with a few drops of a 1mM methanolic NaOH solution. The mixture was allowed to stir for 30 min at ambient temperature and then evaporated to give **13** (13 mg, 97 %) as a glassy solid; (Found: C, 40.25; H, 7.28; 7.79. $C_6H_{13}NO_5$ requires C, 40.22; H, 7.31; N, 7.82%); $[\alpha]^{20}_D$ +11.7° (*c* 0.5, CH_3OH); δ_H (300 MHz, CD_3OD) 4.9-5.3 (m, 1H), 3.5-4.2 (m, 6H); δ_C (75.4 MHz, CD_3OD) 94-101 (1 c), 61-81 (4 c), 51-54 (1 c).

***N*-(*tert*-Butoxycarbonyl)-2,3:6,7-di-*O*-isopropylidene-5-*O*-(*tert*-butyldimethylsilyl)-D-*glycero*-D-*allo*-heptono-1,4-lactam (14).** The title compound was prepared from **8** following the procedure described for compound **9** (33%) as a white solid: mp 122-126°C; (Found: C, 57.39; H, 8.66; N, 2.82. $C_{24}H_{43}NO_8Si$ requires C, 57.46; H, 8.64; N, 2.79%); $[\alpha]^{20}_D$ -20.4° (*c* 0.5, $CHCl_3$); δ_H (300 MHz, $CDCl_3$) 4.80 (d, 1H, *J* = 5.7 Hz), 4.58 (d, 1H, *J* = 5.7 Hz), 4.47 (d, 1H, *J* = 1.3 Hz), 4.07-4.20 (m, 3H), 3.88 (dd, 1H, *J* = 8.4, 5.7 Hz), 1.56 (s, 9H), 1.48 and 1.45 (2s, each 3H), 1.37 (s, 6H), 0.86 (s, 9H), 0.06 and 0.01 (2s, each 3H); δ_C (75.4 MHz, $CDCl_3$) 170.9, 149.6, 111.3, 109.7, 83.4, 77.6, 76.8, 72.5, 72.1, 66.7, 62.3, 27.8, 26.8, 26.0, 25.6, 25.3, 24.6, 17.7, -4.5, -5.1.

1-*O*-Benzoyl-2,3:6,7-di-*O*-isopropylidene-4-[*N*-(*tert*-butoxycarbonylamino)]-5-*O*-(*tert*-butyldimethylsilyl)-4-deoxy-D-*glycero*-D-*allo*-heptitol (15). The title compound was prepared from **14** following the above procedure described to convert **9** into **11** to afford **15** (29%) as an oil; (Found: C, 61.09; H, 8.46; N, 2.32. $C_{31}H_{51}NO_9Si$ requires C, 61.06; H, 8.43; N, 2.30%); $[\alpha]^{20}_D$ -27.6° (*c* 0.8, $CHCl_3$); δ_H (300 MHz, $CDCl_3$) 8.08-8.10 (m, 2H), 7.50-7.57 (m, 1H), 7.40-7.44 (m, 2H), 4.72 (d, 1H, *J* = 10.2 Hz), 4.63-4.67 (bd, 1H), 4.09-4.35 (m, 1H), 4.35 (dd, 1H, *J* = 11.1, 7.2 Hz), 4.19-4.24 (m, 1H), 4.05-4.13 (m, 3H), 3.87 (bt, 1H), 1.49 (s, 3H), 1.43 (s, 12H), 1.35 and 1.33 (2s, each 3H), 0.89 (s, 9H), 0.15 and 0.12 (2s, each 3H); δ_C (75.4 MHz, $CDCl_3$) 166.1, 154.7, 132.7, 129.7, 128.0, 109.0, 108.6, 79.7, 76.5, 75.7, 74.9, 73.7, 67.0, 63.6, 53.6, 28.1, 27.6, 26.2, 25.7, 25.4, 24.8, 17.8, -4.4, -4.6.

2-*O*-(*tert*-Butyldimethylsilyl)-3-[*N*-(*tert*-butoxycarbonylamino)]-4,5-*O*-isopropylidene-6-*O*-benzoyl-3-deoxy-L-allose (16). The title compound was prepared from **15** following the procedure described for compound **12** to afford **16** (65%) as an oil; (Found: C, 60.33; H, 8.05; N, 2.63. $C_{27}H_{43}NO_8Si$ requires C, 60.31; H, 8.06; N, 2.60%); $[\alpha]^{20}_D$ -27.6° (*c* 2.0, $CHCl_3$); δ_H (300 MHz, $CDCl_3$) 9.56 (d, 1H, *J* = 0.6 Hz), 8.05-8.10 (m, 2H), 7.53-7.58 (m, 1H), 7.42-7.49 (m, 2H), 4.69 (bs, 1H), 4.66 (bs, 1H), 4.49 (m, 1H), 4.27-4.36 (m, 3H), 4.22 (bs, 1H), 1.40 (s, 9H), 1.39 and 1.32 (2s, each 3H), 0.96 (s, 9H), 0.12 and 0.09 (2s, each 3H); δ_C (75.4 MHz, $CDCl_3$) 200.2, 166.2, 154.3, 133.4, 132.9, 129.8, 128.3, 109.5, 79.2, 74.9, 73.4, 62.9, 52.9, 28.2, 27.1, 25.7, 25.8, 18.2, -4.6, -5.2.

3-Amino-3-deoxy-L-allose (17). The title compound was prepared from **16** following the procedure described for compound **13** to afford **17** (90%) as a white powder; (Found: C, 40.29; H, 7.37; N, 7.89. $C_6H_{13}NO_5$ requires C, 40.22; H, 7.31; N, 7.82%); $[\alpha]^{20}_D$ -32.9° (*c* 0.3, CH_3OH); hydrochloride salt, mp 160-162°C (decomp.); $[\alpha]^{20}_D$ -27.6° (*c* 0.3, H_2O) {lit.[9] for D-enantiomer, $[\alpha]^{25}_D$ +25° (*c* 0.7, H_2O)}; δ_H (300 MHz, CD_3OD) 5.0 (m, 1H), 3.5-3.9 (m, 5H), 3.44 (m, 1H); δ_C (75.4 MHz, CD_3OD) 95.9, 74.5, 68.3, 64.5, 62.8, 54.8.

***N*-(*tert*-Butoxycarbonyl)-2,3-*O*-isopropylidene-5-*O*-(*tert*-butyldimethylsilyl)-D-*glycero*-D-*talo*-heptono-1,4-lactam (18).** Crystalline lactam **9** (1.5 g, 3.0 mmol) was treated with 70% aq acetic acid and, after being stirred at 40°C for 22 h, the resulting solution was concentrated under reduced pressure. The crude residue was then purified by flash chromatography on silica gel (3:7 hexanes/ethyl acetate) to give 0.94 g (68%) of partially deprotected lactam **18** as a colorless oil; (Found: C, 54.49; H, 8.68; N, 2.91. $C_{21}H_{39}NO_8Si$ requires C, 54.64; H, 8.52; N, 3.03%); $[\alpha]^{20}_D$ +61.15° (*c* 0.4, $CHCl_3$); δ_H (300 MHz, $CDCl_3$) 4.79 (m, 2H), 4.25 (d, 1H, *J* = 4.1 Hz), 4.15 (dd, 1H, *J* = 7.5, 4.1 Hz), 3.74 (m, 1H), 3.51 (m, 2H), 2.83 (bs, 1H), 2.82 (bs, 1H), 1.53 (s, 9H), 1.43 and 1.36 (2s, each 3H), 0.92 (s, 9H), 0.19 and 0.15 (2s, each 3H); δ_C (75.4 MHz, $CDCl_3$) 172.8, 150.3, 111.7, 83.9, 77.7, 73.3, 72.8, 68.2, 63.8, 63.7, 28.0, 26.8, 25.6, 25.2, 17.8, -4.2, -5.0.

2-*O*-(*tert*-Butyldimethylsilyl)-4,5-*O*-isopropylidene-3-[*N*-(*tert*-butoxycarbonylamino)]-3-deoxy-D-altruronic Acid 6,3-Lactam (19). To a solution of lactam **18** (0.9 g, 1.95 mmol) in CH_2Cl_2 (50 mL) was added SiO_2 (230-400 mesh, 2.0 g) and the resulting, vigorously stirred slurry was treated with 0.65M aq $NaIO_4$ (20 mL) at room temperature. After 20 min the slurry was filtered under suction and the silica was washed with ethyl acetate and a few drops of methanol. The filtrates were evaporated under vacuum to leave 0.8 g (95%) of aldehyde **19** as white crystals: mp 140-144°C; (Found: C 55.80; H, 8.34; N, 3.14. $C_{20}H_{35}NO_7Si$ requires C, 55.92; H, 8.21; N, 3.26%); $[\alpha]^{20}_D$ +56.7° (*c* 0.3, $CHCl_3$); δ_H (100 MHz, $CDCl_3$) 9.49 (s, 1H), 4.61 (d, 1H, *J* = 5.5 Hz), 4.52 (d, 1H, *J* = 1.6 Hz), 4.44 (d, 1H, *J* = 5.5 Hz), 4.28 (m, 1H), 1.48 (s, 9H), 1.41 (s, 3H), 1.34 (s, 3H), 0.88 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H); δ_C (25.0 MHz, $CDCl_3$) 199.4, 171.2, 150.1, 111.5, 84.6, 77.8, 77.5, 76.0, 61.8, 27.9, 27.0, 25.7, 25.6, 18.3, -4.1, -5.1.

2,3-*O*-Isopropylidene-4-[*N*-(*tert*-butoxycarbonylamino)]-5-*O*-(*tert*-butyldimethylsilyl)-4-deoxy-D-talose (20). A stirring solution of 0.5 g (1.2 mmol) of aldehyde **19** in dry methanol (8 mL) was cooled at -20°C under nitrogen, and treated with $NaBH_4$ (45 mg, 1.2 mmol). During a period of 3 h, additional portions of $NaBH_4$ were added (3x45 mg, 3x1.2 mmol) while the temperature was allowed to raise to 0°C. After being stirred for a further 1 h, the reaction was quenced by addition of saturated aqueous ammonium chloride (~5 mL), then warmed to room temperature, and vigorously extracted with ethyl acetate (5x5 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure. There was obtained a white crude residue, which was purified by flash chromatography on silica gel (6:4 hexanes/ethyl acetate) affording pure D-talose **20** (β-anomeric pyrrolidinose form) (0.39 g, 78%): white crystals; mp 88-92°C; (Found: C, 55.55; H, 9.26; N, 3.11. $C_{20}H_{39}NO_7Si$ requires C, 55.40; H, 9.07; N, 3.23%); $[\alpha]^{20}_D$ +66.9° (*c* 0.13, $CHCl_3$); δ_H (300 MHz, $CDCl_3$) 5.15 (t, 1H, *J* = 5.7 Hz), 4.62 (t, 1H, *J* = 5.6 Hz), 4.54 (d, 1H, *J* = 5.6 Hz), 4.43 (bs, 1H), 4.10 (m, 1H, exchangeable with D_2O), 3.93 (m, 1H), 3.72 (d, 1H, *J* = 6.1 Hz, exchangeable with D_2O), 3.43 (m, 1H), 3.18 (m, 1H), 1.54 (s, 3H), 1.50 (s, 9H), 1.36 (s, 3H), 0.87 (s, 9H), 0.09 (s, 6H); δ_C (75.4 MHz, $CDCl_3$) 156.2, 111.8, 81.2, 80.7, 80.1, 78.2, 73.6, 62.1, 60.5, 28.2, 25.6, 25.5, 24.7, 17.7, -4.6, -4.7.

4-Amino-4-deoxy-D-talose (21). A solution of protected aminosugar **20** (0.39 g, 0.9 mmol) in 20 mL of a 1:1 mixture of THF and 10% aq HCl was allowed to stir at room temperature for 3 days. The solvent was then removed under vacuum and the residue was treated with a few millilitres of benzene and again evaporated. There was obtained the hydrochloride salt **21** (194 mg, quantitative) as a waxy white solid; (Found: C, 33.50; H, 6.91; N, 6.24. $C_6H_{13}NO_5{\cdot}HCl$ requires C, 33.42; H, 6.54; N, 6.50%); $[\alpha]^{20}_D$ +7.5° (*c* 0.1, methanol); δ_H (300 MHz, D_2O) 5.35 (bs, 0.6H), 4.93 (bs, 0.4H), 4.33 (bt, 0.6H, *J* = 4.1 Hz), 4.21 (t, 0.6H, *J* = 3.4 Hz), 4.11 (t, 0.4H, *J* = 3.9 Hz), 4.05 (m, 0.4H), 3.98 (m, 0.6H), 3.90 (m, 2H), 3.86 (m, 0.4), 3.73 (m, 0.6H), 3.68 (m, 0.4H); δ_C (75.4 MHz, D_2O, major anomer) 74.6, 72.4, 66.6, 66.2, 64.9, 56.0.

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